

=> fil reg

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=> d sta que l36

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^K.VFF^)|(^KK.VFF^)|(^QK.VFF^)|(^HQK.VFF^)|(^HHQK.VFF^)|(^VHHQK
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AQ^)|(^HHQK.VFFAQ^)|(^VHHQK.VFFAQ^)|(^EVHHQK.VFFAQ^)|(^DDDK.VFF
AQ^)/SQSP
L34      104 SEA FILE=REGISTRY ABB=ON  PLU=ON  L33 NOT MULTICHAIN/NTE
L36      102 SEA FILE=REGISTRY ABB=ON  PLU=ON  L34 NOT PMS/CI
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=> d his l36-

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(FILE 'REGISTRY' ENTERED AT 07:09:17 ON 09 MAR 2005)
L36      102 S L34 NOT PMS/CI
        SAV L36 LIU009A/A
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L37      59 S L36
L38      5 S L37 AND (GUPTA A? OR GERVAIS F? OR CHALIFOUR R?)/AU
L39      4 S L37 AND NEUROCHEM?/PA,CS
L40      1 S L37 AND WO2000-CA515/AP,PRN
L41      28 S L37 AND (PD<=20000504 OR PRD<=20000504 OR AD<=20000504)
L42      23 S L37 AND (PD<=19990505 OR PRD<=19990505 OR AD<=19990505)
L43      27 S L38-L40,L42
L44      3 S L41 NOT L43
L45      30 S L43,L44
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L46      76 S E1-E76
        SAV L46 LIU009B/A
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FILE 'HCAPLUS' ENTERED AT 07:19:38 ON 09 MAR 2005

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FILE COVERS 1907 - 9 Mar 2005 VOL 142 ISS 11  
FILE LAST UPDATED: 8 Mar 2005 (20050308/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L45 ANSWER 1 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2004:563390 HCAPLUS  
DN 141:122332  
ED Entered STN: 14 Jul 2004  
TI Amyloid  $\beta$  epitopes, chimeric polypeptides and anti-A $\beta$  antibodies  
for diagnosis and passive immunization treatment of Alzheimer's disease  
IN Schenk, Dale B.  
PA Neuralab Limited, Bermuda  
SO U.S., 79 pp.  
CODEN: USXXAM  
DT Patent  
LA English  
IC ICM C07K016-00  
ICS C07K016-18; A61K039-00  
NCL 424130100; 530300000; 530350000; 530387100  
CC 15-3 (Immunochemistry)  
Section cross-reference(s): 9, 63  
FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	US 6761888	B1	20040713	US 2000-580018	20000526
	US 6750324	B1	20040615	US 2000-724552	20001128 <--
	US 6787637	B1	20040907	US 2000-724551	20001128
	US 2004247591	A1	20041209	US 2004-890070	20040712
	US 2004265301	A1	20041230	US 2004-890000	20040712
	US 2004247590	A1	20041209	US 2004-889999	20040713
PRAI	US 1997-67740P	P	19971202	<--	
	US 1998-80970P	P	19980407	<--	
	US 1998-201430	A2	19981130	<--	
	US 1999-322289	A2	19990528		
	US 2000-580018	A1	20000526		

#### CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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US 6761888	ICM	C07K016-00
	ICS	C07K016-18; A61K039-00
	NCL	424130100; 530300000; 530350000; 530387100
US 6761888	ECLA	A61K039/395
US 6750324	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3;

C07K014/47A3; C07K016/18  
 US 2004247591 ECLA A61K039/395  
 US 2004265301 ECLA A61K039/395  
 US 2004247590 ECLA A61K039/395  
 AB The invention provides improved agents and methods for treatment of diseases associated with amyloid deposits of A $\beta$  in the brain of a patient. Such methods entail administering agents that induce a beneficial immunogenic response against the amyloid deposit. The methods are useful for prophylactic and therapeutic treatment of Alzheimer's disease. Preferred agents including N-terminal fragments of A $\beta$  and antibodies binding to the same.  
 ST beta amyloid epitope chimeric protein antibody Alzheimer disease  
 IT Antibodies and Immunoglobulins  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (IgG1;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Antibodies and Immunoglobulins  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (IgG2;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Antibodies and Immunoglobulins  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (IgG3;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Antibodies and Immunoglobulins  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (IgG4;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Antibodies and Immunoglobulins  
 RL: BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (IgG;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Immunostimulants  
 (adjuvants, Freund's incomplete;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Immunostimulants  
 (adjuvants;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Drug delivery systems  
 (carriers;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Antibodies and Immunoglobulins  
 RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (chimeric;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)  
 IT Mental disorder  
 (cognitive;  $\beta$ -amyloid epitopes, chimeric polypeptides and

- anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Cognition  
(disorder;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(fragments;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(heavy chain;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(humanized;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Diagnosis  
(immunodiagnosis;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(injections, i.m.;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(injections, i.p.;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(injections, i.v.;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(injections, s.c.;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(light chain;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Epitopes  
(mapping;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(monoclonal;  $\beta$ -amyloid epitopes, chimeric polypeptides and

- anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Lipid A  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monophosphates;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(nasal;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(oral;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(polyclonal;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Drug delivery systems  
(topical;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Amyloid  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\beta$ -;  $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Adoptive immunotherapy  
Alzheimer's disease  
Amyloidosis  
B cell (lymphocyte)  
Blood  
Down's syndrome  
Epitopes  
Human  
Phagocytosis  
Protein sequences  
Susceptibility (genetic)  
Test kits  
( $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Amyloid precursor proteins  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)
- IT Antibodies and Immunoglobulins  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
( $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)

- IT Immunoglobulin receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$   
antibodies for diagnosis and passive immunization treatment of  
Alzheimer's disease)
- IT 721870-93-5 721871-28-9 721871-29-0  
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP  
(Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(amino acid sequence;  $\beta$ -amyloid epitopes, chimeric polypeptides  
and anti-A $\beta$  antibodies for diagnosis and passive immunization  
treatment of Alzheimer's disease)
- IT 721871-40-5  
RL: PRP (Properties)  
(unclaimed protein sequence; amyloid  $\beta$  epitopes, chimeric  
polypeptides and anti-A $\beta$  antibodies for diagnosis and passive  
immunization treatment of Alzheimer's disease)
- IT 109796-61-4 111750-71-1 118821-52-6 122630-93-7 123232-50-8  
126779-13-3 126779-14-4 128124-74-3 144500-61-8 158268-86-1  
**176390-00-4** 178949-81-0 184951-43-7 190775-13-4  
192066-10-7 194097-09-1 218133-82-5 252256-37-4 311818-23-2  
311818-25-4 311818-26-5 311818-27-6 311818-28-7 311818-29-8  
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311818-50-5 311818-51-6 311818-52-7 311818-53-8 721398-21-6  
RL: PRP (Properties)  
(unclaimed sequence; amyloid  $\beta$  epitopes, chimeric polypeptides and  
anti-A $\beta$  antibodies for diagnosis and passive immunization  
treatment of Alzheimer's disease)
- IT 107761-42-2, Human  $\beta$ -amyloid peptide-(1-42) 110162-70-4  
214550-60-4 226917-45-9 310901-08-7 311818-15-2 311818-16-3  
311818-17-4 311818-18-5 311818-19-6 311818-20-9 311818-21-0  
312263-67-5 721398-20-5 721870-94-6 721870-95-7 721870-96-8  
721870-97-9 721870-98-0 721870-99-1 721871-00-7 721871-01-8  
RL: BSU (Biological study, unclassified); DGN (Diagnostic use); PRP  
(Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$   
antibodies for diagnosis and passive immunization treatment of  
Alzheimer's disease)
- IT 7784-30-7, Aluminum phosphate 21645-51-2, Aluminum hydroxide, biological  
studies 141256-04-4, QS 21  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
( $\beta$ -amyloid epitopes, chimeric polypeptides and anti-A $\beta$   
antibodies for diagnosis and passive immunization treatment of  
Alzheimer's disease)

RE.CNT 393 THERE ARE 393 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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RL: PRP (Properties)

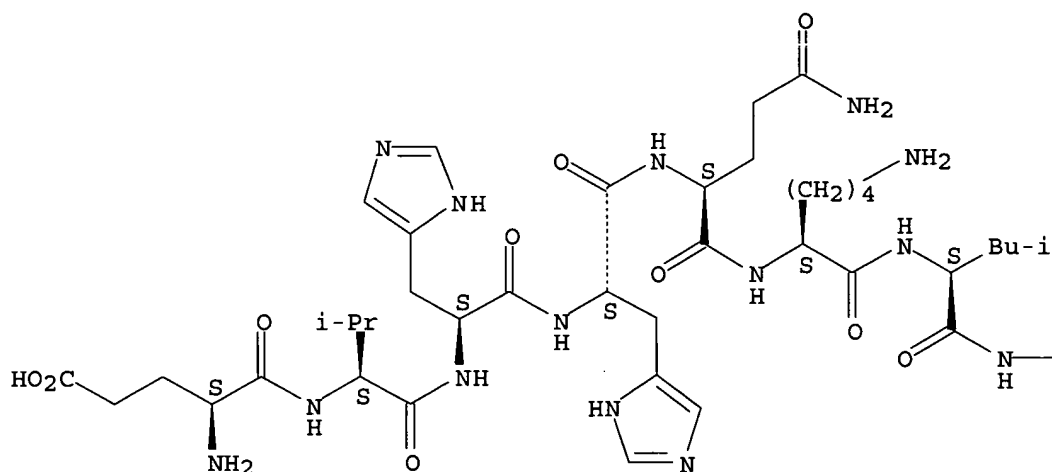
(unclaimed sequence; amyloid  $\beta$  epitopes, chimeric polypeptides and anti-A $\beta$  antibodies for diagnosis and passive immunization treatment of Alzheimer's disease)

RN 176390-00-4 HCAPLUS

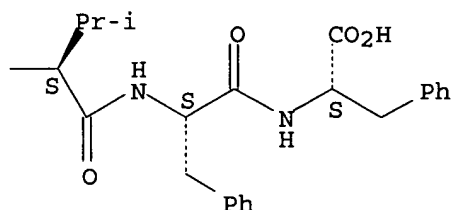
CN L-Phenylalanine, L- $\alpha$ -glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutamyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L45 ANSWER 2 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2003:701932 HCAPLUS  
 DN 139:301297  
 ED Entered STN: 08 Sep 2003  
 TI Stereoselective Interactions of Peptide Inhibitors with the  $\beta$ -Amyloid Peptide  
 AU Chalifour, Robert J.; McLaughlin, Richard W.; Lavoie, Louis; Morissette, Celine; Tremblay, Nadine; Boule, Marie; Sarazin, Philippe; Stea, Dino; Lacombe, Diane; Tremblay, Patrick; Gervais, Francine  
 CS Neurochem Inc., Saint-Laurent, QC, H4S 2A1, Can.  
 SO Journal of Biological Chemistry (2003), 278(37), 34874-34881  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 CC 1-3 (Pharmacology)  
 AB Residues 16-20 of the  $\beta$ -amyloid peptide ( $A\beta$ ) function as a self-recognition element during  $A\beta$  assembly into fibers. Peptides containing this motif retain the ability to interact with  $A\beta$  and, in some cases, potentially inhibit its assembly. Replacing L- with D-amino acids could stabilize such peptides and permit their evaluation as therapeutic agents for Alzheimer's disease. Here we have assessed the effect that such a chiral reversal has on inhibitory potency. D-enantiomers of five peptides, KLVFFA, KKLVFFA, KVFVFA, KIVFFA, and KVVFFA, were unexpectedly more active as inhibitors in an in vitro fibrillogenesis assay. CD showed that D-KLVFFA more effectively prevented  $A\beta$  adopting the  $\beta$ -sheet secondary structure correlated with fibrillogenesis. Electron microscopy showed that fiber formation was also more strongly inhibited by D-KLVFFA. Heterochiral inhibition was confirmed using D- $A\beta$ , on the principle that enantiomeric proteins exhibit reciprocal chiral biochem. interactions. With D- $A\beta$ , L-KLVFFA was the more potent inhibitor, rather than D-KLVFFA. Most significantly, D-peptides were more potent at reducing the toxicity of both  $A\beta$ 1-40 and  $A\beta$ 1-42 toward neuronal cells in culture. This unforeseen heterochiral stereoselectivity of  $A\beta$  for D-peptide inhibitors should be considered during future design of peptide-based inhibitors of  $A\beta$  neurotoxicity and fibrillogenesis.  
 ST stereoselective interaction peptide inhibitor beta amyloid peptide; Alzheimers disease treatment peptide  
 IT Organelle  
 (fibril, inhibition of fibrillogenesis; stereoselective interactions of

- peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Self-assembly  
(inhibition of A $\beta$  assembly; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Conformational transition  
 $\beta$ -Sheet  
(inhibition of A $\beta$  transition to  $\beta$ -sheet secondary structure; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Cytoprotective agents  
(neuroprotective, protection against neurotoxicity of A $\beta$ ; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Nerve  
Neurotoxicity  
(protection against neurotoxicity of A $\beta$ ; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Alzheimer's disease  
Anti-Alzheimer's agents  
Human  
Structure-activity relationship  
(stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Nerve  
(toxicity, protection against neurotoxicity of A $\beta$ ; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT Amyloid  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
( $\beta$ -; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT 9005-49-6, Heparin, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibition of heparin-promoted A $\beta$  fibrillogenesis; stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT 107761-42-2, Amyloid  $\beta$  1-42 131438-79-4, Amyloid  $\beta$  peptide(1-40) (synthetic)  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)
- IT 190775-14-5 206198-57-4 307299-71-4  
307299-72-5 307299-75-8 342877-55-8  
342877-57-0 342877-58-1 342877-59-2  
342877-64-9  
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 190775-14-5

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

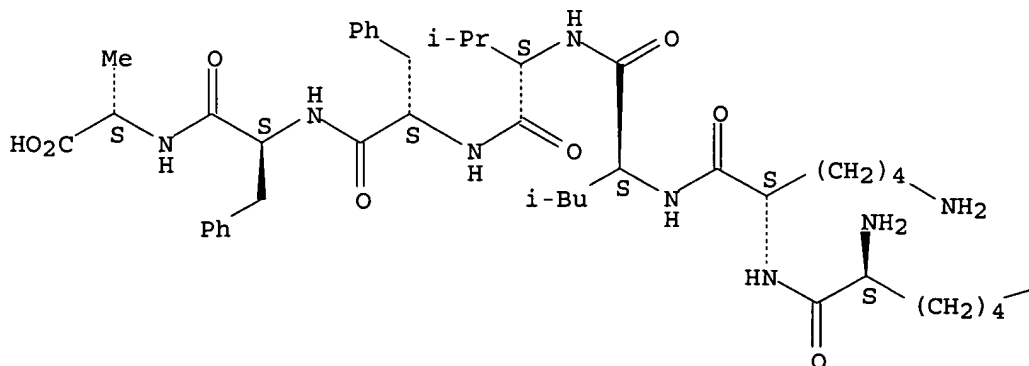
(stereoselective interactions of peptide inhibitors with the  $\beta$ -amyloid peptide in relation to Alzheimer's disease treatment)

RN 190775-14-5 HCAPLUS

CN L-Alanine, L-lysyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A





PAGE 1-B

—NH<sub>2</sub>

L45 ANSWER 3 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
AN 2002:770145 HCAPLUS  
DN 137:284351  
ED Entered STN: 10 Oct 2002  
TI Peptides and pharmaceutical compositions thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits  
IN Soto-Jara, Claudio; Baumann, Marc H.; Frangione, Blas  
PA New York University, USA  
SO U.S., 51 pp., Cont.-in-part of U.S. 5,948,763.  
CODEN: USXXAM

DT Patent  
LA English

IC ICM A61K038-00  
ICS C07K016-00

NCL 530326000

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 1

FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6462171	B1	20021008	US 1996-766596	19961212 <--
	US 5948763	A	19990907	US 1996-630645	19960410 <--
	US 2003087407	A1	20030508	US 2002-235483	20020906 <--
PRAI	US 1995-478326	B2	19950607	<--	
	US 1996-630645	A2	19960410	<--	
	US 1996-766596	A1	19961212	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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US 6462171	ICM	A61K038-00
	ICS	C07K016-00
	NCL	530326000

US 6462171	ECLA	A61K049/00H6; C07K005/08H2A; C07K014/47A3; G01N033/68V2
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US 5948763	ECLA	A61K049/00H6; C07K005/08H2A; C07K014/47A3; G01N033/68V2
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US 2003087407	ECLA	A61K049/00H6; C07K005/08H2A; C07K014/47A3; G01N033/68V2
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AB Novel peptides capable of interacting with a hydrophobic  $\beta$ -sheet forming cluster of amino acid residues on a protein or peptide for amyloid or amyloid-like deposit formation inhibit and structurally block the abnormal folding of proteins and peptides into amyloid or amyloid-like deposits and into pathol.  $\beta$ -sheet-rich conformation as precursors thereof. Methods for preventing, treating or detecting disorders or diseases associated with amyloid-like fibril deposits, such as Alzheimer's disease and prion-related encephalopathies, are also provided.

ST peptide protein folding inhibitor amyloid prion disease

IT Drug delivery systems  
(carriers; peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

IT Prion diseases  
Protein folding  
Protein sequences  
(peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

IT Amyloid  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
(peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

IT Amyloid  
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
( $\beta$ -; peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

IT Amino acids, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(D-; peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

IT 112805-81-9 148439-49-0 162470-97-5 162471-00-3 167396-02-3  
182912-63-6 182912-66-9 182912-70-5 182912-72-7 182912-74-9  
182912-76-1 186606-30-4 186606-34-8 186606-39-3 186606-43-9  
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186606-80-4 186606-84-8 186606-88-2 186606-93-9 186606-96-2  
186607-00-1 186607-04-5 186607-08-9 186607-12-5 186607-15-8  
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464892-75-9 464892-76-0 464892-77-1 **464892-78-2**  
464892-79-3 464892-80-6 464892-82-8 464892-84-0 464892-85-1  
464892-86-2 464892-87-3 464892-88-4 464892-90-8 464892-91-9  
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

IT 152286-31-2 173692-60-9 467233-47-2 467233-48-3 467233-49-4  
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467233-55-2 467233-56-3 467233-57-4 467233-58-5 467233-59-6  
467233-60-9 467233-61-0 467233-62-1 467233-63-2  
RL: PRP (Properties)  
(unclaimed sequence; peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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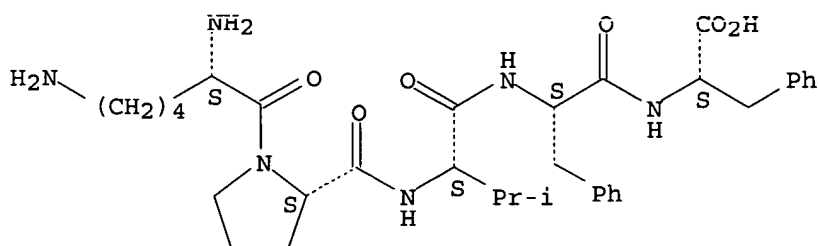
IT 464892-78-2

RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (peptides and pharmaceutical compns. thereof for treatment of disorders or diseases associated with abnormal protein folding into amyloid or amyloid-like deposits)

RN 464892-78-2 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-prolyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 4 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:540135 HCAPLUS

DN 137:108295

ED Entered STN: 19 Jul 2002

TI Vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases

IN Chalifour, Robert; Hebert, Lise; Kong, Xianqi; Gervais, Francine

PA Can.

SO U.S. Pat. Appl. Publ., 28 pp., Cont.-in-part of U.S. Ser. No. 724,842.  
 CODEN: USXXCO

DT Patent

LA English

IC ICM A61K039-00

NCL 424185100

CC 15-2 (Immunochemistry)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002094335	A1	20020718	US 2001-867847	20010529
	WO 2002096937	A2	20021205	WO 2002-CA763	20020529
	WO 2002096937	A3	20030710		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,				

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, US, UZ, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,  
 GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,  
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 EP 1392728 A2 20040303 EP 2002-729715 20020529  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 PRAI US 1999-168594P P 19991129  
 US 2000-724842 A2 20001128  
 US 2001-867847 A 20010529  
 WO 2002-CA763 W 20020529

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002094335	ICM	A61K039-00
	NCL	424185100
US 2002094335	ECLA	A61K039/00D3; C07K014/47A3; C07K016/18
AB		The present invention relates to a stereochem. based "non-self" antigen vaccine for the prevention and/or treatment of Alzheimer's and other amyloid related diseases. The present invention provides a vaccine for the prevention and treatment of Alzheimer's and other amyloid related diseases, which overcomes the drawbacks associated with using naturally occurring peptides, proteins or immunogens. The vaccine comprises fibril peptides consisting of all- D-amino acids.
ST		D amino acid fibril peptide amyloid related disease; Alzheimer disease vaccine nonself fibril peptide
IT		Gene, animal
		RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
		(APP; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Brain, disease
		Prion diseases
		(Creutzfeldt-Jakob; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Proteins
		RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
		(SAA (serum amyloid A), serum; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Functional groups
		(acid; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Macrophage
		(adherence region; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Functional groups
		(alkoxy groups; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Functional groups
		(alkoxycarbonyl groups; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Functional groups
		(alkoxyphosphonyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Functional groups
		(alkyloxysulfonyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)
IT		Brain, disease

(amyloid angiopathy; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(aryloxycarbonyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(aryloxyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(carbamyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Toxicity  
(cellular; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Infection  
Inflammation  
(chronic; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Proteins  
RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(conjugates; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Nervous system, disease  
(degeneration; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Amyloidosis  
(familial Mediterranean fever; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Fever and Hyperthermia  
(familial Mediterranean; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Organelle  
(fibril, formation inhibition; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Proteins  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(fibril; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Antibodies and Immunoglobulins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(heavy chain; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Dialysis  
(hemodialysis; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(hydroxycarbonyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Antibodies and Immunoglobulins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(light chain; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(lower alkyl; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Brain, disease  
Prion diseases

(mad cow; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Diabetes mellitus  
(non-insulin-dependent; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Antigens  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(non-self; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Hormones, animal, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptide; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Salts, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(pharmaceutical acceptable; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Esters, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(pharmaceutical acceptable; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(phosphono; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(precursor, fibril; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Prion proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(precursor; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Brain, disease  
Prion diseases  
(scrapie; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Mutagenesis  
(site-directed, deletion; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Mutagenesis  
(site-directed, insertion; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Mutagenesis  
(site-directed, substitution; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Functional groups  
(sulfo group; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Acyl groups  
Alzheimer's disease  
Amino group  
Amyloidosis  
Drug delivery systems  
Epitopes

Human  
 Hydroxyl group  
 Peptidomimetics  
 Prion diseases  
 Rheumatoid arthritis  
 Tuberculosis  
 Vaccines  
 $\beta$ -Sheet  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Antibodies and Immunoglobulins  
 RL: BPN (Biosynthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Amyloid precursor proteins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Aromatic compounds  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Gelsolin  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Heterocyclic compounds  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Keratins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Transthyretin  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Fibrinogens  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ( $\alpha$  chain; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Microglobulins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 ( $\beta$ -microglobulins; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT Amino acids, biological studies  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (D-; vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT 165196-29-2 342877-52-5 342877-53-6 342877-54-7 342877-55-8  
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342877-99-0 342878-00-6 342878-01-7 342878-02-8 342878-03-9

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RL: BSU (Biological study, unclassified); PRP (Properties); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)

(vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT 9001-63-2, Lysozyme 85637-73-6, Atrial natriuretic peptide 91448-99-6, Cystatin C 106602-62-4, Islet amyloid polypeptide 216864-07-2D,  $\alpha$ -Synuclein, derivs. 216864-08-3D,  $\beta$ -Synuclein, derivs.

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)

(vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

IT 342877-55-8

RL: BSU (Biological study, unclassified); PRP (Properties); THU

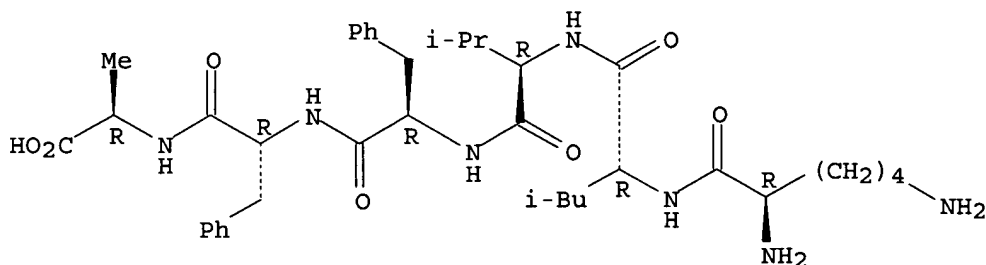
(Therapeutic use); BIOL (Biological study); USES (Uses)

(vaccines comprising all-D fibril peptides for prevention and treatment of Alzheimer's and amyloid-related diseases)

RN 342877-55-8 HCAPLUS

CN D-Alanine, D-lysyl-D-leucyl-D-valyl-D-phenylalanyl-D-phenylalanyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 5 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2002:89879 HCAPLUS

DN 136:139864

ED Entered STN: 01 Feb 2002

TI Amyloid targeting imaging agents

IN Gervais, Francine; Kong, Xianqi; Chalifour, Robert;  
Migneault, David

PA Neurochem, Inc., Can.

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K051-04

ICS A61K051-08

CC 63-6 (Pharmaceuticals)

Section cross-reference(s): 8

FAN.CNT 2



	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2002007781	A2	20020131	WO 2001-CA1071	20010725	
	WO 2002007781	A3	20021031			
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
	US 2002115717	A1	20020822	US 2001-915092	20010724	
	CA 2416617	AA	20020131	CA 2001-2416617	20010725	
	EP 1303311	A2	20030423	EP 2001-956226	20010725	
	R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR		
	NO 2003000397	A	20030324	NO 2003-397	20030124	
PRAI	US 2000-220808P	P	20000725			
	US 2001-915092	A	20010724			
	WO 2001-CA1071	W	20010725			

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
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WO 2002007781	ICM	A61K051-04
	ICS	A61K051-08
US 2002115717	ECLA	A61K051/04Z; A61K051/08Z

OS MARPAT 136:139864

AB Amyloid-targeting imaging agents such as radiolabeled amyloid targeting mols. and amyloid targeting mol.-chelator conjugates for imaging, e.g., amyloid plaques in vivo, and/or for the treatment of amyloidosis disorders are described. The invention provides amyloid-targeting imaging agents that are useful for imaging sites of amyloid disease. The imaging agents are capable of binding specifically to amyloid plaques, as an aid in diagnosis and/or early treatment of amyloidosis disorders.

ST amyloid targeting imaging agent; amyloidosis imaging agent; peptide radionuclide complex imaging agent

IT Brain, disease

Prion diseases

(Creutzfeldt-Jakob; amyloid targeting imaging agents)

IT Imaging

(acoustic; amyloid targeting imaging agents)

IT Brain, disease

(amyloid angiopathy; amyloid targeting imaging agents)

IT Alzheimer's disease

Amyloidosis

Buffers

Diagnosis

Imaging agents

Radiopharmaceuticals

Reducing agents

(amyloid targeting imaging agents)

IT Amyloid

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(amyloid targeting imaging agents)

IT Chelates

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)

(amyloid targeting imaging agents)

IT Radionuclides, biological studies

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);

USES (Uses)

(imaging agents labeled with; amyloid targeting imaging agents)

IT Brain, disease  
Prion diseases  
(kuru; amyloid targeting imaging agents)

IT Brain, disease  
Prion diseases  
(mad cow; amyloid targeting imaging agents)

IT Diabetes mellitus  
(non-insulin-dependent; amyloid targeting imaging agents)

IT Peptides, biological studies  
RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);  
USES (Uses)  
(radiolabeled conjugates; amyloid targeting imaging agents)

IT Brain, disease  
Prion diseases  
(scrapie; amyloid targeting imaging agents)

IT 100-88-9D, Cyclohexylsulfamic acid, radiolabeled conjugates 573-58-0D,  
Congo red, radiolabeled conjugates 959-81-9D, radiolabeled conjugates  
1119-23-9D, radiolabeled conjugates 1119-25-1D, radiolabeled conjugates  
1119-71-7D, radiolabeled conjugates 1119-93-3D, radiolabeled conjugates  
1119-95-5D, radiolabeled conjugates 1119-96-6D, radiolabeled conjugates  
1119-98-8D, radiolabeled conjugates 1119-99-9D, radiolabeled conjugates  
1120-00-9D, radiolabeled conjugates 1120-03-2D, radiolabeled conjugates  
1120-05-4D, radiolabeled conjugates 1138-84-7D, radiolabeled conjugates  
1829-00-1D, Thiazol yellow g, radiolabeled conjugates 2390-54-7D,  
Thioflavin t, radiolabeled conjugates 2610-05-1D, Chicago sky blue 6B,  
radiolabeled conjugates 2785-06-0D, radiolabeled conjugates  
3095-95-2D, radiolabeled conjugates 3119-93-5D, radiolabeled conjugates  
3785-01-1D, radiolabeled conjugates 4033-31-2D, radiolabeled conjugates  
4443-32-7D, radiolabeled conjugates 4444-23-9D, radiolabeled conjugates  
4481-44-1D, radiolabeled conjugates 4720-61-0D, radiolabeled conjugates  
10043-49-9D, Au 198, imaging agents labeled with 10043-66-0D, I 131,  
imaging agents labeled with 10098-91-6D, Y 90, imaging agents labeled  
with 10098-97-2D, Sr 90, imaging agents labeled with 10198-40-0D, Co  
60, imaging agents labeled with 13501-35-4D, radiolabeled conjugates  
13967-65-2D, Ho 166, imaging agents labeled with 13981-25-4D, imaging  
agents labeled with 13981-50-5D, Co 57, imaging agents labeled with  
13981-56-1D, Fluorine 18, imaging agents labeled with 14119-09-6D, Ga  
67, imaging agents labeled with 14158-27-1D, Sr 89, imaging agents  
labeled with 14158-31-7D, I 125, imaging agents labeled with  
14276-65-4D, Gd-153, imaging agents labeled with 14378-26-8D,  
Rhenium-188, imaging agents labeled with 14391-11-8D, Au 199, imaging  
agents labeled with 14392-02-0D, Cr 51, imaging agents labeled with  
14913-89-4D, Rh 105, imaging agents labeled with 14933-09-6D,  
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201, imaging agents labeled with 15214-89-8D, radiolabeled conjugates  
15715-08-9D, I 123, imaging agents labeled with 15750-15-9D, imaging  
agents labeled with 15757-86-5D, Copper-67, imaging agents labeled with  
15758-35-7D, imaging agents labeled with 15766-00-4D, Sm 153, imaging  
agents labeled with 20694-16-0 29777-99-9D, radiolabeled conjugates  
38878-02-3D, radiolabeled conjugates 40265-71-2D, radiolabeled  
conjugates 42457-53-4D, radiolabeled conjugates 42846-15-1D,  
radiolabeled conjugates 49625-94-7D, radiolabeled conjugates  
50567-35-6D, radiolabeled conjugates 52962-42-2D, radiolabeled  
conjugates 58431-88-2D, radiolabeled conjugates 63555-51-1D,  
radiolabeled conjugates 63585-09-1D, radiolabeled conjugates  
72943-20-5D, radiolabeled conjugates 75708-92-8D, Folic acid dihydrate,  
radiolabeled conjugates 76936-63-5D, radiolabeled conjugates  
77337-76-9D, radiolabeled conjugates 80969-51-3D, radiolabeled  
conjugates 82611-83-4D, radiolabeled conjugates 83678-67-5,  
Gadolinium-DOTA 92014-92-1D, radiolabeled conjugates 101373-15-3D,  
radiolabeled conjugates 153247-40-6D, radiolabeled conjugates

176390-19-5D, radiolabeled conjugates 176390-21-9D, radiolabeled conjugates  
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 256954-44-6D, radiolabeled conjugates 256954-45-7D, radiolabeled conjugates  
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 342877-55-8D, radiolabeled conjugates 374068-19-6D, radiolabeled conjugates  
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 393175-29-6D, radiolabeled conjugates 393175-41-2D, radiolabeled conjugates  
 393175-43-4D, radiolabeled conjugates 393175-46-7D, radiolabeled conjugates  
 393175-50-3D, radiolabeled conjugates 393175-52-5D, radiolabeled conjugates  
 393175-54-7D, radiolabeled conjugates 393175-56-9D, radiolabeled conjugates  
 393175-58-1D, radiolabeled conjugates 393175-60-5D, radiolabeled conjugates  
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 393175-74-1D, radiolabeled conjugates 393175-76-3D, radiolabeled conjugates  
 393175-78-5D, radiolabeled conjugates 393175-88-7D, radiolabeled conjugates  
 393176-17-5D, radiolabeled conjugates 393176-41-5D, radiolabeled conjugates  
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 393176-58-4D, radiolabeled conjugates 393176-60-8D, radiolabeled conjugates  
 393176-63-1D, radiolabeled conjugates 393176-65-3D, radiolabeled conjugates  
 393176-67-5D, radiolabeled conjugates 393176-68-6D, radiolabeled conjugates  
 393176-70-0D, radiolabeled conjugates 393176-72-2D, radiolabeled conjugates  
 393176-74-4D, radiolabeled conjugates 393176-76-6D, radiolabeled conjugates

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);  
 USES (Uses)

(amyloid targeting imaging agents)

IT 14133-76-7D, imaging agents labeled with 14885-78-0D, imaging agents  
 labeled with

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);  
 USES (Uses)

(metastable; amyloid targeting imaging agents)

IT 153247-40-6D, radiolabeled conjugates

RL: DGN (Diagnostic use); THU (Therapeutic use); BIOL (Biological study);

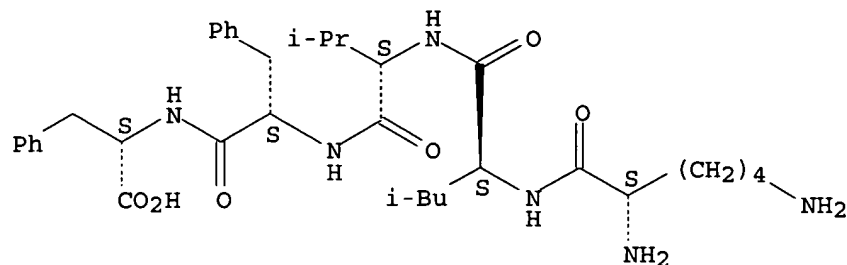
## USES (Uses)

(amyloid targeting imaging agents)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 6 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:844884 HCAPLUS

DN 136:665

ED Entered STN: 21 Nov 2001

TI Modified peptide modulators of amyloid aggregation

IN Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; Reed, Michael J.

PA Praecis Pharmaceuticals Incorporated, USA

SO U.S., 54 pp., Cont.-in-part of U.S. Ser. No. 548,998, abandoned.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K038-02

ICS A61K038-17; C07K001-113; C07K014-47

NCL 424094300

CC 1-11 (Pharmacology)

Section cross-reference(s): 9, 34, 63

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
PI	US 6319498	B1	20011120	US 1996-617267	19960314 <--
	US 5817626	A	19981006	US 1995-404831	19950314 <--
	US 5854215	A	19981229	US 1995-475579	19950607 <--
	AU 759036	B2	20030403	AU 2000-35389	20000519 <--
	US 2002098173	A1	20020725	US 2001-972475	20011004 <--
	AU 769915	B2	20040212	AU 2002-15539	20020211 <--
	US 2004005307	A1	20040108	US 2003-463729	20030617 <--
PRAI	US 1995-404831	A2	19950314	<--	
	US 1995-475579	A2	19950607	<--	
	US 1995-548998	B2	19951027	<--	
	AU 1996-52524	A3	19960314	<--	
	US 1996-617267	A1	19960314	<--	
	AU 1997-42387	A3	19970827	<--	
	US 2001-972475	A1	20011004		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
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US 6319498	ICM	A61K038-02	
	ICS	A61K038-17; C07K001-113; C07K014-47	
	NCL	424094300	
US 6319498	ECLA	C07K014/47A3	<--

US 5817626 ECLA C07K014/47A3 <--  
 US 5854215 ECLA C07K014/47A3 <--  
 US 2002098173 ECLA C07K014/47A3 <--  
 US 2004005307 ECLA C07K014/47A3 <--

OS MARPAT 136:665

AB Compds. that modulate the aggregation of amyloidogenic proteins or peptides are disclosed. The modulators of the invention can promote amyloid aggregation or, more preferably, can inhibit natural amyloid aggregation. In a preferred embodiment, the compds. modulate the aggregation of natural  $\beta$  amyloid peptides ( $\beta$ -AP). In a preferred embodiment, the  $\beta$  amyloid modulator compds. are comprised of an A $\beta$  aggregation core domain and a modifying group coupled thereto such that the compound alters the aggregation or inhibits the neurotoxicity of natural  $\beta$  amyloid peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural  $\beta$ -AP aggregation when the natural  $\beta$ -APs are in a molar excess amount relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compds. of the invention, are also disclosed.

ST peptide deriv prepn amyloid aggregation modulation; amyloidogenic disease peptide deriv amyloid aggregation modulation

IT Amyloid  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (A, modified; modified peptide modulators of amyloid aggregation)

IT Apolipoproteins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (A-I, modified; modified peptide modulators of amyloid aggregation)

IT Proteins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (amyloidogenic, modified; modified peptide modulators of amyloid aggregation)

IT Antibodies and Immunoglobulins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (light chain,  $\kappa$  and  $\lambda$ , modified; modified peptide modulators of amyloid aggregation)

IT Drug delivery systems  
 Nerve  
 Neurotoxicity  
 Pharmacokinetics  
 (modified peptide modulators of amyloid aggregation)

IT Amyloid  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (modified peptide modulators of amyloid aggregation)

IT Fibrinogens  
 Gelsolin  
 Peptides, biological studies  
 Prion proteins  
 Transthyretin  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (modified; modified peptide modulators of amyloid aggregation)

IT Peptides, biological studies  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (retro-inverso; modified peptide modulators of amyloid aggregation)

IT Nerve  
 (toxicity; modified peptide modulators of amyloid aggregation)

IT Amyloid

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
( $\beta$ -; modified peptide modulators of amyloid aggregation)

IT Microglobulins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\beta$ 2-, modified; modified peptide modulators of amyloid aggregation)

IT Amino acids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(D-; modified peptide modulators of amyloid aggregation)

IT 81-25-4, Cholic acid  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(modified peptide modulators of amyloid aggregation)

IT 183745-81-5DP, biotinylated 350032-71-2DP, biotinylated  
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(modified peptide modulators of amyloid aggregation)

IT 2577-40-4D, N-terminal cholyl derivs. 10183-34-3D, N-terminal cholyl derivs. 13116-21-7D, N-terminal cholyl derivs. 64533-15-9D, N-terminal cholyl derivs. 123529-23-7 123529-23-7D, N-terminal derivs. 134649-29-9D, N-terminal cholyl derivs. 152286-31-2D, N-terminal cholyl derivs. 153247-40-6 153247-40-6D, N-terminal cholyl derivs. 153247-40-6D, iminobiotinylated 153247-42-8D, N-terminal cholyl derivs. 156858-22-9 173923-64-3D, N-terminal cholyl derivs. 176390-00-4D, N-terminal cholyl derivs. 176390-02-6D, N-terminal cholyl derivs. 176390-05-9D, N-terminal cholyl derivs. 176390-09-3D, N-terminal cholyl derivs. 176390-14-0D, N-terminal cholyl derivs. 176390-18-4D, N-terminal cholyl derivs. 176390-24-2D, N-terminal cholyl derivs. 182912-78-3 182912-78-3D, N-terminal cholyl derivs. 182912-79-4D, N-terminal cholyl derivs. 183745-81-5 183745-81-5D, N-terminal derivs. 183745-82-6 183745-82-6D, N-terminal conjugates 183746-61-4 183746-61-4D, N-terminal cholyl derivs. 183746-61-4D, N-terminal derivs. 183746-77-2 183746-77-2D, N-terminal cholyl derivs. 183746-96-5 183746-98-7 183746-98-7D, N-terminal derivs. 183746-99-8 183746-99-8D, N-terminal derivs. 183906-01-6 183906-04-9 183906-05-0 183906-07-2 183906-08-3 183906-09-4 183906-10-7 183906-12-9 192699-33-5D, N-terminal cholyl derivs. 204333-52-8D, N-terminal cholyl derivs. 250370-63-9D, N-terminal cholyl derivs. 321913-13-7D, N-terminal cholyl derivs. 362652-21-9 362652-21-9D, N-terminal derivs. 365537-59-3D, N-terminal cholyl derivs. 365537-60-6D, N-terminal cholyl derivs. 365537-61-7D, N-terminal cholyl derivs. 365537-62-8D, N-terminal cholyl derivs. 365537-63-9D, N-terminal cholyl derivs. 365537-64-0D, N-terminal cholyl derivs. 365537-65-1D, N-terminal cholyl derivs. 365537-66-2D, N-terminal cholyl derivs. 374068-10-7D, N-terminal cholyl derivs. 374068-11-8D, N-terminal cholyl derivs. 374068-12-9D, N-terminal cholyl derivs. 374068-13-0D, N-terminal cholyl derivs. 374068-14-1D, N-terminal cholyl derivs. 374068-15-2D, N-terminal cholyl derivs. 374068-16-3D, N-terminal cholyl derivs. 374068-17-4D, N-terminal cholyl derivs. 374068-18-5D, N-terminal cholyl derivs. 374068-19-6D, N-terminal cholyl derivs. 374068-20-9D, N-terminal derivs. 374068-21-0D, N-terminal cholyl derivs. 374068-22-1D, N-terminal cholyl derivs. 374068-23-2D, N-terminal cholyl derivs. 374068-24-3D, N-terminal cholyl derivs. 374068-25-4D, N-terminal cholyl derivs.  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(modified peptide modulators of amyloid aggregation)

IT 9001-63-2D, Lysozyme, modified 9007-12-9D, Calcitonin, modified 56645-65-9D, Procalcitonin, modified 85637-73-6D, Atrial natriuretic factor, modified 91448-99-6D, Cystatin C, modified 106602-62-4D, Islet amyloid polypeptide, modified

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(modified peptide modulators of amyloid aggregation)

IT 183745-81-5D, resin-bound  
RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)  
(modified peptide modulators of amyloid aggregation)

IT 58-85-5, Biotin  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction; modified peptide modulators of amyloid aggregation)

IT 134500-80-4 169593-16-2 365537-65-1 374068-23-2 375376-36-6  
375798-27-9  
RL: PRP (Properties)  
(unclaimed protein sequence; modified peptide modulators of amyloid aggregation)

IT 10183-34-3 **176390-05-9 176390-09-3 176390-14-0**  
176390-18-4 182912-79-4 183486-00-2 192699-33-5 **206198-57-4**  
250370-63-9 250370-72-0 **365537-51-5 365537-52-6**  
365537-59-3 365537-60-6 365537-61-7 365537-62-8 365537-63-9  
365537-64-0 365537-66-2 374068-18-5 **374068-21-0**  
374068-22-1 374068-24-3 374068-25-4 375376-34-4 375376-38-8  
375376-40-2 375376-41-3 375376-42-4  
RL: PRP (Properties)  
(unclaimed sequence; modified peptide modulators of amyloid aggregation)

RE.CNT 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

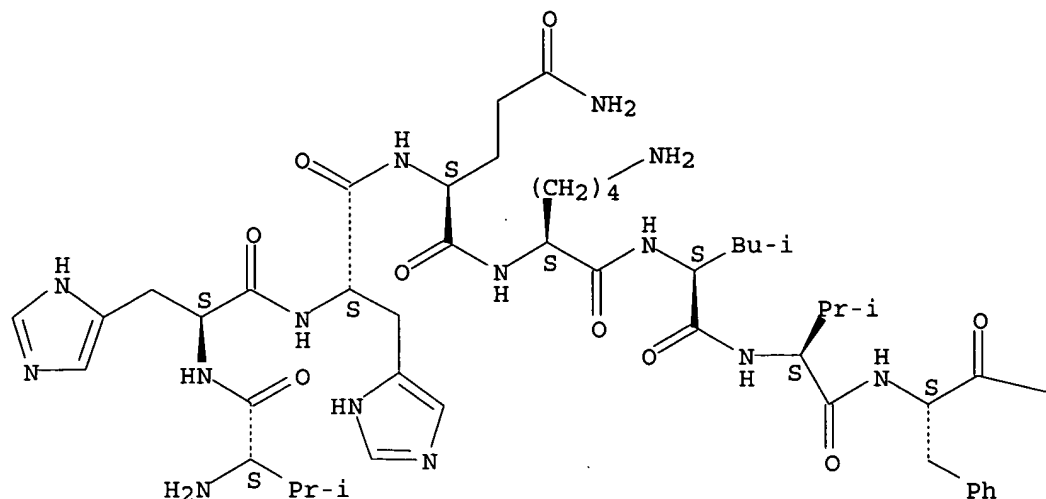
- (1) Anon; EP 464549 1992 HCAPLUS
- (2) Anon; EP 554887 A1 1993 HCAPLUS
- (3) Anon; WO 9304194 1993 HCAPLUS
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IT 134649-29-9D, N-terminal cholyl derivs.  
RL: BSU (Biological study, unclassified); PRP (Properties); THU  
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(modified peptide modulators of amyloid aggregation)  
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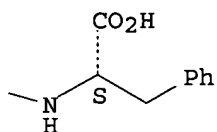
Absolute stereochemistry.



PAGE 1-A



PAGE 1-B



L45 ANSWER 7 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:757810 HCAPLUS  
 DN 135:298818  
 ED Entered STN: 17 Oct 2001  
 TI D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation  
 IN Findeis, Mark A.; Gefter, Malcolm L.; Musso, Gary; Signer, Ethan R.; Wakefield, James; Molineaux, Susan; Chin, Joseph; Lee, Jung-Ja; Kelley, Michael; Komar-Panicucci, Sonja; Arico-Muendel, Christopher C.; Phillips, Kathryn; Hayward, Neil J.  
 PA Praecis Pharmaceuticals, Inc., USA  
 SO U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 616,081.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K038-06  
 ICS A61K038-07; A61K038-08; A61K038-10  
 NCL 514002000

CC 1-12 (Pharmacology)

Section cross-reference(s): 34, 63

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6303567	B1	20011016	US 1996-703675	19960827 <--
	US 5817626	A	19981006	US 1995-404831	19950314 <--
	US 5854215	A	19981229	US 1995-475579	19950607 <--
	CA 2262453	AA	19980305	CA 1997-2262453	19970827 <--
	WO 9808868	A1	19980305	WO 1997-US15166	19970827 <--
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	RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9742387	A1	19980319	AU 1997-42387	19970827 <--
	AU 741199	B2	20011122		
	EP 929574	A1	19990721	EP 1997-940663	19970827 <--
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	US 6277826	B1	20010821	US 1999-356931	19990719 <--
	AU 759036	B2	20030403	AU 2000-35389	20000519 <--
	US 2002103134	A1	20020801	US 2001-895443	20010629 <--
	US 6689752	B2	20040210		
	AU 769915	B2	20040212	AU 2002-15539	20020211 <--
PRAI	US 1995-404831	A2	19950314	<--	
	US 1995-475579	A2	19950607	<--	
	US 1995-548998	B2	19951027	<--	
	US 1996-616081	B2	19960314	<--	
	AU 1996-52524	A3	19960314	<--	
	US 1996-703675	A	19960827	<--	
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	AU 1997-42387	A3	19970827	<--	
	US 1997-920162	A1	19970827	<--	
	WO 1997-US15166	W	19970827	<--	
	US 1999-356931	A1	19990719		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6303567	ICM	A61K038-06
	ICS	A61K038-07; A61K038-08; A61K038-10
	NCL	514002000
US 6303567	ECLA	C07K014/47A3 <--
US 5817626	ECLA	C07K014/47A3 <--
US 5854215	ECLA	C07K014/47A3 <--
WO 9808868	ECLA	C07K014/47A3 <--
US 5985242	ECLA	C07K014/47A3 <--
US 6277826	ECLA	C07K014/47A3 <--
US 2002103134	ECLA	C07K014/47A3 <--

OS MARPAT 135:298818

AB Comps. that modulate natural  $\beta$  amyloid peptide aggregation are provided. The modulators of the invention comprise a peptide, preferably based on a  $\beta$  amyloid peptide, that is comprised entirely of D-amino acids. Preferably, the peptide comprises 3-5 D-amino acid residues and includes at least two D-amino acid residues independently selected from D-leucine, D-phenylalanine, and D-valine. In a particularly preferred embodiment, the peptide is a retro-inverso isomer of a  $\beta$  amyloid peptide, preferably a retro-inverso isomer of A $\beta$ 17-21. In certain

embodiments, the peptide is modified at the amino-terminus, the carboxyl-terminus, or both. Preferred amino-terminal modifying groups include cyclic, heterocyclic, polycyclic and branched alkyl groups. Preferred carboxyl-terminal modifying groups include an amide group, an alkyl amide group, an aryl amide group, and a hydroxy group. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases (e.g. Alzheimer's disease) using the compds. of the invention, are also disclosed.

- ST D amino acid peptide amyloid modulator; Alzheimer disease D amino acid peptide; retro inverso peptide amyloid modulator
- IT Biological transport  
(drug; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Cytoprotective agents  
(neuroprotectants; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Toxicity  
(neurotoxicity; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Cerebrospinal fluid  
(peptide stability in; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(retro-inverso; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Nerve  
(toxicity; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Amyloid  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
( $\beta$ -; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Aggregation  
( $\beta$ -amyloid peptide; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Amino acids, biological studies  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(D-; D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Drug delivery systems  
Pharmacokinetics  
(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- IT 26305-03-3P, Pepstatin A 183746-33-0P 183746-58-9P 183746-91-0P  
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365538-47-2P 365538-48-3P 365538-50-7P 365538-51-8P 365538-52-9P

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 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)

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 365537-20-8 365537-21-9 365537-22-0 365537-23-1 365537-24-2  
 365537-25-3 365537-26-4 365537-27-5 365537-28-6 365537-28-6D, iodo  
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 365537-31-1 365537-32-2 365537-32-2D, iodo derivative 365537-33-3  
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 365537-55-9 365537-55-9D, amino- and carboxyl-terminal modified derivs.  
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 365537-66-2D, modifying group derivs. 365537-67-3 365537-67-3D,  
 derivs. 365537-68-4

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
 study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide  
 aggregation)

IT 365537-68-4D, derivs. 365537-69-5 365537-69-5D, derivs. 365537-71-9  
 365537-73-1 365537-75-3 365537-77-5 365537-78-6 365537-78-6D,  
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amino-terminal modified derivs. 365538-14-3D, modifying group derivs.  
365538-17-6D, modifying group derivs. 365538-20-1D, modifying group  
derivs. 365538-23-4D, modifying group derivs. 365538-28-9D, modifying  
group derivs. 365538-31-4D, modifying group derivs. 365538-34-7D,  
modifying group derivs. 365538-37-0D, modifying group derivs.  
365538-38-1D, modifying group derivs. 365538-39-2D, modifying group  
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365538-42-7 365538-43-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological  
study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide  
aggregation)

IT 176390-05-9 176390-09-3 176390-18-4 182912-78-3  
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RL: PRP (Properties)

(D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide  
aggregation)

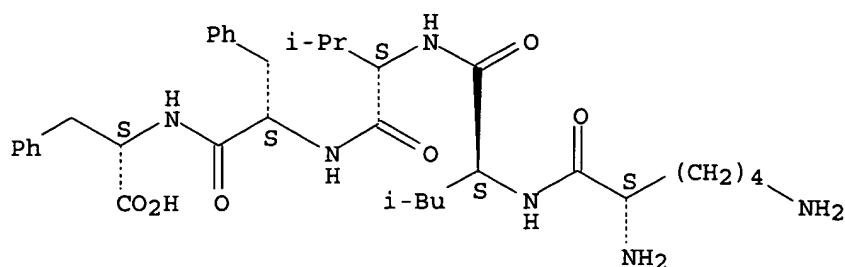
RE.CNT 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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- IT 153247-40-6D, stereoisomer  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (D-amino acid-containing peptide modulators of  $\beta$ -amyloid peptide aggregation)
- RN 153247-40-6 HCAPLUS
- CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L45 ANSWER 8 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:526090 HCAPLUS

DN 135:92861

ED Entered STN: 20 Jul 2001

TI Process for the preparation of N $\alpha$ -2-(4-nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides

IN Kim, Hack-Joo; Chweh, Weonu; Kim, Young-Cheol

PA Hyundai Pharmaceutical Ind. Co., Ltd., S. Korea

SO PCT Int. Appl., 23 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K005-00

CC 34-3 (Amino Acids, Peptides, and Proteins)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001051505	A1	20010719	WO 1999-KR810	19991224 <--
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRAI	WO 1999-KR810		19991224 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001051505	ICM	C07K005-00
WO 2001051505	ECLA	C07C317/18; C07K001/06A2; C07K001/08D <--

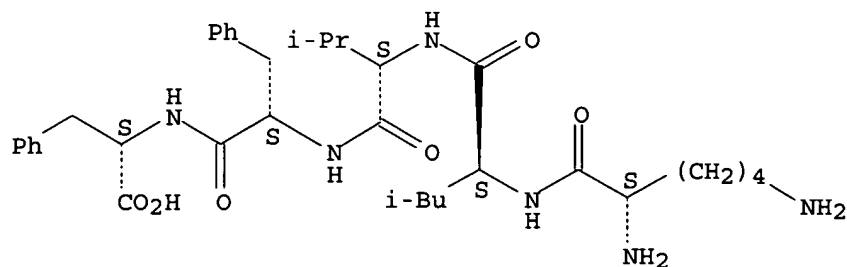
OS CASREACT 135:92861; MARPAT 135:92861

AB Title amino acid fluorides p-O<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>SO<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>O<sub>2</sub>CNR<sub>1</sub>CHR<sub>2</sub>COF [R<sub>1</sub> = H, R<sub>2</sub> = H, iso-Pr, 2-methylpropyl, tert-butoxymethyl, benzyl, 2-(tert-butoxycarbonyl)ethyl, 4-(tert-butoxycarbamido)butyl or 4-tert-butoxybenzyl] (Nsc-amino acid fluorides) were prepared by fluorinating Nsc-amino acids with cyanuric fluoride. Thus, 1 mmol Nsc-Val-OH in CH<sub>2</sub>Cl<sub>2</sub> was treated with 3 mmol cyanuric fluoride and 1 mmol dry pyridine under nitrogen for 30 min to afford 82% Nsc-Val-F. The Nsc-amino acids fluorides were applied, without an activation step, to the solid-phase synthesis of peptides Leu-enkephalin, A-VI-5 peptide, and  $\beta$ -amyloid peptide.

ST nitrophenylsulfonylethoxycarbonyl amino acid fluoride prepn peptide coupling

IT Solid phase synthesis  
(peptide; preparation of (nitrophenylsulfonyl)ethoxycarbonyl amino acid fluorides)

Absolute stereochemistry.



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L45 ANSWER 9 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:416788 HCAPLUS
DN 135:18553
ED Entered STN: 08 Jun 2001
TI Vaccine for the prevention and treatment of Alzheimer's and amyloid
related diseases
IN Chalifour, Robert; Hebert, Lise; Kong, Xianqi; Gervais,
Francine
PA Neurochem, Inc., Can.
SO PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K039-00
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CC 15-2 (Immunochemistry)

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001039796	A2	20010607	WO 2000-CA1413	20001129
	WO 2001039796	A3	20011206		
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	CA 2388559	AA	20010607	CA 2000-2388559	20001129
	BR 2000016022	A	20020806	BR 2000-16022	20001129
	EP 1235587	A2	20020904	EP 2000-981111	20001129
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
	JP 2004500354	T2	20040108	JP 2001-541528	20001129
	NO 2002002531	A	20020712	NO 2002-2531	20020528
PRAI	US 1999-168594P	P	19991129		
	US 2000-724842	A	20001128		
	WO 2000-CA1413	W	20001129		

## CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	WO 2001039796	ICM	A61K039-00
	JP 2004500354	FTERM	4C085/AA03; 4C085/BB11; 4C085/CC32; 4C085/EE06; 4C085/FF02; 4C085/FF13; 4C085/FF14; 4C085/FF19; 4C085/GG02; 4C085/GG03; 4C085/GG04; 4C085/GG08; 4C085/GG10; 4H045/AA10; 4H045/AA30; 4H045/BA01; 4H045/BA11; 4H045/BA12; 4H045/BA13; 4H045/BA14; 4H045/BA18; 4H045/BA19; 4H045/CA40; 4H045/EA31
AB	The present invention relates to a stereochem. based "non-self" antigen vaccine for the prevention and/or treatment of Alzheimer's and other amyloid related diseases. The present invention provides a vaccine for the prevention and treatment of Alzheimer's and other amyloid related diseases, which overcomes the drawbacks associated with using naturally occurring peptides, proteins or immunogens.		
ST	vaccine Alzheimers disease amyloidosis D peptide antibody		
IT	Peptides, biological studies		
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)		
	(all-D; vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)		
IT	Organelle		
	(fibril; vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)		
IT	Alzheimer's disease		
	Amyloidosis		
	Self-association		
	Vaccines		
	(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)		
IT	Antibodies		
	RL: BAC (Biological activity or effector, except adverse); BPN		

(Biosynthetic preparation); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

IT Amyloid

RL: BSU (Biological study, unclassified); BIOL (Biological study) (β-; vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

IT 165196-29-2P 226707-64-8P 342877-52-5P 342877-53-6P 342877-54-7P  
 342877-55-8P 342877-56-9P 342877-57-0P  
 342877-58-1P 342877-59-2P 342877-60-5P  
 342877-61-6P 342877-62-7P 342877-63-8P  
 342877-64-9P 342877-65-0P 342877-66-1P  
 342877-67-2P 342877-68-3P 342877-69-4P  
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 342877-76-3P 342877-77-4P 342877-78-5P 342877-79-6P 342877-80-9P  
 342877-81-0P 342877-82-1P 342877-83-2P 342877-84-3P 342877-85-4P  
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 342896-25-7P 342896-48-4P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

IT 342877-55-8P

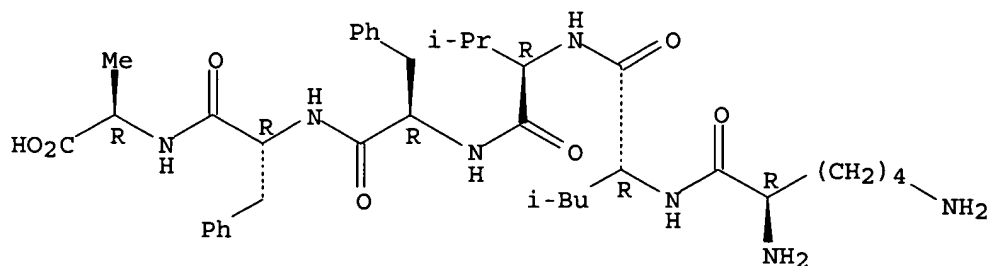
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(vaccine for prevention and treatment of Alzheimer's and amyloid related diseases using all-D peptides that elicit immune response to amyloid protein)

RN 342877-55-8 HCAPLUS

CN D-Alanine, D-lysyl-D-leucyl-D-valyl-D-phenylalanyl-D-phenylalanyl- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



DN 134:125971  
 ED Entered STN: 02 Feb 2001  
 TI Peptides containing N-substituted D-amino acids for preventing  
 $\beta$ -strand association  
 IN Stott, Kelvin  
 PA UK  
 SO PCT Int. Appl., 76 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-47  
 ICS A61K038-17; A61P025-28; C07K007-06  
 CC 1-12 (Pharmacology)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2001007474	A1	20010201	WO 2000-GB2923	20000728 <--	
	W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
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	AU 767396	B2	20031106	AU 2000-63004	20000728 <--	
PRAI	GB 1999-17725	A	19990728	<--		
	WO 2000-GB2923	W	20000728			

## CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	WO 2001007474	ICM	C07K014-47
		ICS	A61K038-17; A61P025-28; C07K007-06
AB	Chemical compds. and compns. are disclosed which comprise peptides composed of D-enantiomers of amino acids and capable of binding to $\beta$ -strand structures to form $\beta$ -sheets, the peptides being selectively N $\alpha$ -substituted to prevent further $\beta$ -strand association. The peptides are useful for preventing $\beta$ -strand association. The capacity of all-D-[Ac--Leu-MeLeu-Leu-MeLeu-Arg-Arg-NH <sub>2</sub> ] to inhibit aggregation of a synthetic peptide fragment corresponding to residues 11-25 of the Alzheimer A $\beta$ peptide into amyloid fibrils was determined.		
ST	peptide deriv beta strand assocn inhibition; Alzheimer amyloid aggregation inhibition peptide		
IT	Proteins, general, biological studies		
	RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)		
	(aggregation; peptides containing N-substituted D-amino acids for preventing $\beta$ -strand association)		
IT	Cytotoxic agents		
	(conjugates; peptides containing N-substituted D-amino acids for preventing $\beta$ -strand association)		
IT	Antibodies		
	Enzymes, biological studies		
	Hormones, animal, biological studies		
	Proteins, specific or class		
	Transcription factors		

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (conjugates; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Biological transport  
 (drug; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Electrostatic force  
 (electrostatic and other non-covalent interactions; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Hydrophobicity  
 (hydrophobic interaction; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Aggregation  
 Anti-Alzheimer's agents  
 Blood-brain barrier  
 Chromophores  
 Drug targeting  
 Fluorescent substances  
 Hydrogen bond  
 Immobilization, biochemical  
 Magnetic materials  
 Molecular association  
 Radioactive substances  
 Spectroscopy  
 Spin labels  
 (peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Peptides, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Amino acids, biological studies  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
 (peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Amyloid  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Conformation  
 (protein; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Amyloid  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 ( $\beta$ -; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT Conformation  
 ( $\beta$ -strand; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT 321909-16-4P  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
 (peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT 56-40-6, Glycine, biological studies    56-41-7, L-Alanine, biological studies    56-87-1, L-Lysine, biological studies    60-18-4, L-Tyrosine,

biological studies 61-90-5, L-Leucine, biological studies 63-68-3, L-Methionine, biological studies 63-91-2, L-Phenylalanine, biological studies 71-00-1, L-Histidine, biological studies 72-18-4, L-Valine, biological studies 73-22-3, L-Tryptophan, biological studies 73-32-5, L-Isoleucine, biological studies 74-79-3, L-Arginine, biological studies 147-85-3, L-Proline, biological studies 153-94-6, D-Tryptophan 157-06-2, D-Arginine 312-84-5, D-Serine 319-78-8, D-Isoleucine 328-38-1, D-Leucine 338-69-2, D-Alanine 348-67-4, D-Methionine 351-50-8, D-Histidine 556-02-5, D-Tyrosine 556-02-5D, D-Tyrosine, derivs. 632-20-2, D-Threonine 640-68-6, D-Valine 673-06-3, D-Phenylalanine 673-06-3D, D-Phenylalanine, derivs. 921-01-7, D-Cysteine 923-27-3, D-Lysine 1783-96-6, D-Aspartic acid 2058-58-4, D-Asparagine 2280-48-0, D- $\beta$ -Hydroxyvaline 5959-95-5, D-Glutamine 6893-26-1, D-Glutamic acid 26782-71-8, D-tert-Leucine  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT 153247-41-7

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT 2564-83-2, TEMPO 3229-53-6, PROXYL 7553-56-2D, Iodine, isotopes, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

IT 153247-40-6 321985-33-5 321985-34-6

RL: PRP (Properties)  
(unclaimed sequence; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Chitnumsub, P; BIOORGANIC AND MEDICINAL CHEMISTRY 1999, V7(1), P39 HCAPLUS
- (2) Doig, A; CHEM COMMUN (CAMBRIDGE) 1997, 22, P2153 HCAPLUS
- (3) Findeis, E; BIOCHEMISTRY 1999, V38(21), P6791
- (4) Pallitto, M; BIOCHEMISTRY 1999, V38(12), P3570 HCAPLUS
- (5) Pharm Peptides Inc; WO 9628471 A 1996 HCAPLUS
- (6) Praecis Pharm Inc; WO 0052048 A 2000 HCAPLUS
- (7) Texas A & M University Syst; WO 9746547 A 1997 HCAPLUS
- (8) Tjernberg, L; JOURNAL OF BIOLOGICAL CHEMISTRY 1997, V272(19), P12601

MEDLINE

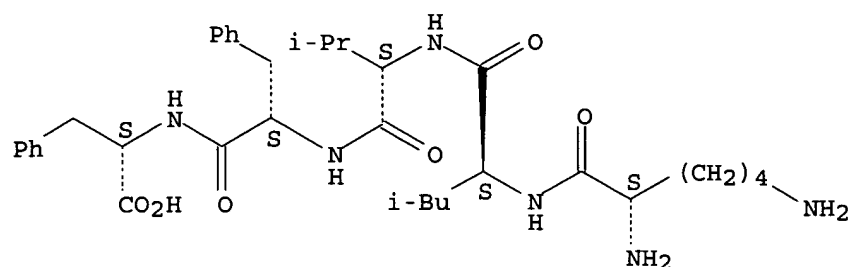
IT 153247-40-6

RL: PRP (Properties)  
(unclaimed sequence; peptides containing N-substituted D-amino acids for preventing  $\beta$ -strand association)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 11 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2001:78414 HCAPLUS  
 DN 134:141772  
 ED Entered STN: 02 Feb 2001  
 TI Peptides containing N-substituted L-amino acids for preventing  
 $\beta$ -strand association  
 IN Stott, Kelvin  
 PA UK  
 SO PCT Int. Appl., 77 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-47  
 ICS A61K038-17; A61P025-28; C07K007-06  
 CC 1-12 (Pharmacology)  
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001007473	A1	20010201	WO 2000-GB2901	20000728 <--
W:			AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
CA 2378779	AA	20010201	CA 2000-2378779	20000728 <--
EP 1203019	A1	20020508	EP 2000-948175	20000728 <--
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL	
JP 2003505469	T2	20030212	JP 2001-512556	20000728 <--
AU 766992	B2	20031030	AU 2000-61737	20000728 <--
NZ 516441	A	20031128	NZ 2000-516441	20000728 <--
PRAI GB 1999-17724	A	19990728	<--	
WO 2000-GB2901	W	20000728		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001007473	ICM	C07K014-47
	ICS	A61K038-17; A61P025-28; C07K007-06

AB Chemical compds. and compns. are disclosed which comprise peptides capable of binding to  $\beta$ -strand structures to form  $\beta$ -sheets, the peptides being selectively  $N\alpha$ -substituted to prevent further  $\beta$ -strand association. The peptides are useful for preventing  $\beta$ -strand association. The capacity of Ac-Arg-MeArg-Leu-MeLeu-Phe-MePhe-NH<sub>2</sub> to inhibit aggregation of a synthetic peptide fragment corresponding to residues 11-25 of the Alzheimer A $\beta$  peptide into amyloid fibrils was determined.



- ST peptide deriv beta strand assocn inhibition; Alzheimer amyloid aggregation inhibition peptide
- IT Proteins, general, biological studies  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (aggregation; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Cytotoxic agents  
 (conjugates; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Antibodies  
 Enzymes, biological studies  
 Hormones, animal, biological studies  
 Proteins, specific or class  
 Transcription factors  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (conjugates; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Biological transport  
 (drug; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Aggregation  
 Anti-Alzheimer's agents  
 Blood-brain barrier  
 Chromophores  
 Drug targeting  
 Fluorescent substances  
 Immobilization, biochemical  
 Magnetic materials  
 Molecular association  
 Molecular modeling  
 Radioactive substances  
 Spectroscopy  
 Spin labels  
 (peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Peptides, biological studies  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Amino acids, biological studies  
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
 (peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Amyloid  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Conformation  
 (protein; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Amyloid  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 ( $\beta$ -; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT Conformation  
 ( $\beta$ -strand; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)

- IT Amino acids, biological studies  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(D-; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 321909-10-8P  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 9001-92-7, Protease  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 52-90-4, L-Cysteine, biological studies 56-40-6, Glycine, biological studies 56-41-7, L-Alanine, biological studies 56-45-1, L-Serine, biological studies 56-84-8, L-Aspartic acid, biological studies 56-85-9, L-Glutamine, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 60-18-4, L-Tyrosine, biological studies 60-18-4D, L-Tyrosine, derivs., biological studies 61-90-5, L-Leucine, biological studies 63-68-3, L-Methionine, biological studies 63-91-2, L-Phenylalanine, biological studies 63-91-2D, L-Phenylalanine, derivs., biological studies 70-47-3, L-Asparagine, biological studies 71-00-1, L-Histidine, biological studies 72-18-4, L-Valine, biological studies 72-19-5, L-Threonine, biological studies 73-22-3, L-Tryptophan, biological studies 73-32-5, L-Isoleucine, biological studies 74-79-3, L-Arginine, biological studies 147-85-3, L-Proline, biological studies 2280-28-6,  $\beta$ -Hydroxyvaline 33105-81-6, tert-Leucine  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 153247-41-7  
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 2564-83-2, TEMPO 3229-53-6, PROXYL 7553-56-2D, Iodine, isotopes, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 322422-25-3  
RL: PRP (Properties)  
(unclaimed protein sequence; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)
- IT 153247-40-6 321982-76-7  
RL: PRP (Properties)  
(unclaimed sequence; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Chitnumsub, P; BIOORGANIC AND MEDICINAL CHEMISTRY 1999, V7(1), P39 HCAPLUS
- (2) Doig, A; CHEM COMMUN (CAMBRIDGE) 1997, 22, P2153 HCAPLUS
- (3) Findeis, E; BIOCHEMISTRY 1999, V38(21), P6791
- (4) Karolinska Innovations Ab; WO 9721728 A 1997 HCAPLUS
- (5) Moehle, K; JOURNAL OF PEPTIDE RESEARCH 1998, V51(1), P19
- (6) Pallitto, M; BIOCHEMISTRY 1999, V38(12), P3570 HCAPLUS
- (7) Pharm Peptides Inc; WO 9628471 A 1996 HCAPLUS

(8) Texas A & M University Syst; WO 9746547 A 1997 HCAPLUS

IT 153247-40-6

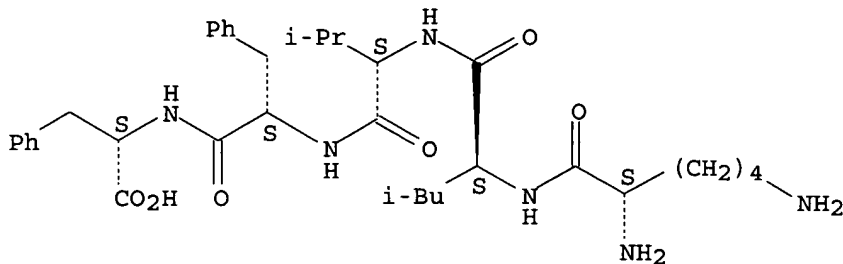
RL: PRP (Properties)

(unclaimed sequence; peptides containing N-substituted L-amino acids for preventing  $\beta$ -strand association)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 12 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:861520 HCAPLUS

DN 134:28433

ED Entered STN: 08 Dec 2000

TI Prevention and treatment of amyloidogenic disease

IN Schenk, Dale B.; Bard, Frederique; Vasquez, Nicki J.; Yednock, Ted

PA Neuralab Limited, Bermuda

SO PCT Int. Appl., 143 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K039-395

ICS A61K038-17; A61K039-39; A61K039-00; G01N033-68; A61K048-00;

A61P025-28; C07K016-18; C07K014-47

CC 15-2 (Immunochemistry)

Section cross-reference(s): 8, 63

FAN.CNT 9

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000072880	A2	20001207	WO 2000-US14810	20000526
	WO 2000072880	A3	20010531		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2370311	AA	20001207	CA 2000-2370311	20000526
	BR 2000011000	A	20020219	BR 2000-11000	20000526
	EP 1185298	A2	20020313	EP 2000-937919	20000526
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200103447	T2	20020422	TR 2001-200103447	20000526
	GB 2368794	A1	20020515	GB 2001-30969	20000526
	GB 2368794	B2	20041020		
	DE 10084643	T	20020711	DE 2000-10084643	20000526

TR 200202231	T2	20021121	TR 2002-200202231	20000526
EE 200100626	A	20030217	EE 2001-626	20000526
JP 2003517461	T2	20030527	JP 2001-511319	20000526
NZ 515403	A	20040528	NZ 2000-515403	20000526
US 6710226	B1	20040323	US 2000-723384	20001127 <--
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ZA 2001009487	A	20030217	ZA 2001-9487	20011116
NO 2001005773	A	20020125	NO 2001-5773	20011127
BG 106241	A	20020830	BG 2001-106241	20011219
US 2005009150	A1	20050113	US 2002-232030	20020830 <--
US 2004265308	A1	20041230	US 2004-788666	20040227 <--
US 2004219146	A1	20041104	US 2004-828548	20040419 <--
US 2005013815	A1	20050120	US 2004-923471	20040820 <--
US 2005019330	A1	20050127	US 2004-923469	20040820 <--
US 2005048049	A1	20050303	US 2004-923474	20040820 <--
PRAI US 1999-322289	A2	19990528		
US 1997-67740P	P	19971202	<--	
US 1998-80970P	P	19980407	<--	
US 1998-201430	A2	19981130	<--	
US 2000-580015	A1	20000526		
WO 2000-US14810	W	20000526		
US 2000-723713	A2	20001127		
US 2000-724319	A3	20001127		
US 2000-251892P	P	20001206		
US 2001-10942	A1	20011206		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000072880	ICM ICS	A61K039-395 A61K038-17; A61K039-39; A61K039-00; G01N033-68; A61K048-00; A61P025-28; C07K016-18; C07K014-47
GB 2368794	ECLA	A61K039/00D; A61K039/00D3; C07K014/47A3; C07K016/18
US 6710226	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3; C07K014/47A3; C07K016/18 <--
US 6743427	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3; C07K014/47A3; C07K016/18 <--
US 2005009150	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3; C07K014/47A3; C07K016/18 <--
US 2004265308	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3; C07K014/47A3; C07K016/18 <--
US 2004219146	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3; C07K014/47A3; C07K016/18 <--
US 2005019330	ECLA	A61K038/17A2; A61K038/19B+M; A61K039/00D3; C07K014/47A3; C07K016/18 <--
AB		The invention provides improved agents and methods for treatment of diseases associated with amyloid deposits of A $\beta$ in the brain of a patient. Such methods entail administering agents that induce a beneficial immunogenic response against the amyloid deposit. The methods are useful for prophylactic and therapeutic treatment of Alzheimer's disease. Preferred agents including N-terminal fragments of A $\beta$ and antibodies binding to the same.
ST		amyloid beta epitope antibody Alzheimer disease; amyloidogenic disease
IT		Phagocytosis (Fc receptor-mediated; N-terminal fragments of amyloid $\beta$ and antibodies for prevention and treatment of amyloidogenic disease)
IT		Immunoglobulins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (G1; N-terminal fragments of amyloid $\beta$ and antibodies for prevention and treatment of amyloidogenic disease)
IT		Immunoglobulins RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL

(Biological study); USES (Uses)  
(G2; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(G3; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(G4; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Alzheimer's disease  
Animal tissue  
Blood  
Down's syndrome  
Epitopes  
Labels  
Mammal (Mammalia)  
NMR tomography  
Phagocyte  
Protein sequences  
Susceptibility (genetic)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulin receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Amyloid precursor proteins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Antigens  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Fusion proteins (chimeric proteins)  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Peptides, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Polynucleotides  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Proteins, general, biological studies  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Alums  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES

(Uses)  
 (N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Antibodies  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunostimulants  
 (adjuvants, Freund's incomplete; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunostimulants  
 (adjuvants; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Diagnosis  
 (agents, kit; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Brain, disease  
 Disease, animal  
 (amyloidogenic; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Mouse  
 (antibody; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
 (carriers; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Mental disorder  
 (cognitive; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Amyloid  
 RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)  
 (deposit; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Test kits  
 (diagnostic; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Extracellular matrix  
 (disease; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Cognition  
 (disorder; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (fragments; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins  
 RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (heavy chains; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Diagnosis  
 (immunodiagnosis; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
 (injections, i.m.; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
 (injections, i.v.; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
 (injections, s.c.; N-terminal fragments of amyloid  $\beta$  and

antibodies for prevention and treatment of amyloidogenic disease)

IT Paramagnetic materials  
(label; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Immunoglobulins  
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(light chains; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Antibodies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monoclonal; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Lipid A  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(monophosphates; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
(nasal, intra-; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
(oral; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Disease, animal  
(proliferative; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
(solns., i.p.; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
(sustained-release; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Infection  
Inflammation  
Neoplasm  
(tissue sample; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Drug delivery systems  
(topical; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT Amyloid  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
( $\beta$ -; N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT 107761-42-2, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety)  
118427-80-8 214550-64-8 250741-37-8 268202-35-3 310901-06-5  
310901-07-6  
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT 141256-04-4, QS-21 310901-08-7 312273-37-3  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(N-terminal fragments of amyloid  $\beta$  and antibodies for prevention and treatment of amyloidogenic disease)

IT 178949-81-0 214550-60-4 226917-45-9 311818-22-1  
RL: PRP (Properties)  
(Unclaimed; prevention and treatment of amyloidogenic disease)

IT 109796-61-4 110162-70-4 111750-71-1 118821-52-6 122630-93-7  
123232-50-8 126779-13-3 126779-14-4 128124-74-3 144500-61-8

158268-86-1 176390-00-4 184951-43-7 190775-13-4  
 192066-10-7 194097-09-1 218133-82-5 252256-37-4 311818-14-1  
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 311818-20-9 311818-21-0 311818-23-2 311818-25-4 311818-26-5  
 311818-27-6 311818-28-7 311818-29-8 311818-30-1 311818-31-2  
 311818-32-3 311818-33-4 311818-34-5 311818-35-6 311818-36-7  
 311818-37-8 311818-38-9 311818-39-0 311818-40-3  
 311818-41-4 311818-42-5 311818-43-6 311818-44-7 311818-45-8  
 311818-46-9 311818-47-0 311818-48-1 311818-49-2 311818-50-5  
 311818-51-6 311818-52-7 311818-53-8 311860-14-7 312273-39-5  
 312273-40-8 312273-41-9 312273-49-7 312273-58-8 312277-40-0  
 312277-41-1 312277-42-2 312277-43-3 312277-56-8

RL: PRP (Properties)

(unclaimed sequence; prevention and treatment of amyloidogenic disease)

IT 176390-00-4

RL: PRP (Properties)

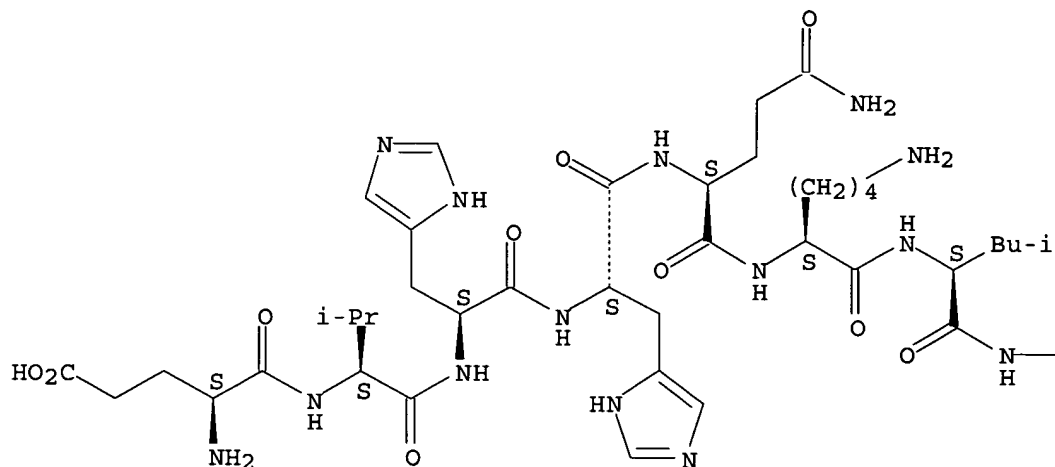
(unclaimed sequence; prevention and treatment of amyloidogenic disease)

RN 176390-00-4 HCAPLUS

CN L-Phenylalanine, L- $\alpha$ -glutamyl-L-valyl-L-histidyl-L-histidyl-L-glutamyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

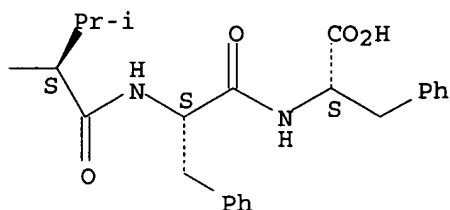
Absolute stereochemistry.

PAGE 1-A





PAGE 1-B



L45 ANSWER 13 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 2000:814515 HCAPLUS  
 DN 133:361912  
 ED Entered STN: 21 Nov 2000  
 TI Stereoselective antifibrillogenic peptides and peptidomimetics thereof  
 IN Chalifour, Robert; Gervais, Francine; Gupta, Ajay  
 PA Neurochem, Inc., Can.  
 SO PCT Int. Appl., 46 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-47  
 ICS A61K038-17; G01N033-68; A61P025-28; C12N005-00; A61K051-00  
 CC 15-2 (Immunochemistry)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000068263	A2	20001116	WO 2000-CA515	20000504 <--
	WO 2000068263	A3	20010503		
	W:				
	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW:				
	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	CA 2388092	AA	20001116	CA 2000-2388092	20000504 <--
	EP 1173480	A2	20020123	EP 2000-926599	20000504 <--
	R:				
	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2003503312	T2	20030128	JP 2000-616237	20000504 <--
PRAI	US 1999-132592P	P	19990505	<--	
	WO 2000-CA515	W	20000504	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2000068263	ICM	C07K014-47

ICS A61K038-17; G01N033-68; A61P025-28; C12N005-00;  
A61K051-00

- AB The present invention relates to antifibrillogenic agents for inhibiting amyloidosis and/or for cytoprotection for the treatment of amyloidosis disorders. These agents include peptides, isomers thereof and peptidomimetic compds. thereof. These agents comprise a peptide having a sequence identified from the glycosaminoglycan (GAG) binding region and the prot-prot interaction region of the amyloid protein. The peptide has at least one D-amino acid isomer substitution. The invention also relates to the peptide bound to a label for in vivo imaging of amyloid deposits.
- ST antifibrillogenic peptidomimetic amyloid protein amyloidosis; retroinverso peptide antifibrillogenic agent Alzheimer disease
- IT Drugs  
(antifibrillogenic peptides; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Peptides, biological studies  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(antifibrillogenic; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Drug delivery systems  
(carriers; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Transplant and Transplantation  
(cell; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Peptides, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(conjugates; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Amyloid  
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)  
(deposit detection; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Organelle  
(fibril, formation inhibition; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Amino acids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(hydrophobic; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Peptides, biological studies  
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(retro-inverso; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Alzheimer's disease  
Amyloidosis  
Imaging agents  
Labels  
Mammal (Mammalia)  
Peptidomimetics  
Protein sequences  
(stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Animal cell  
(transplant; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT Amino acids, biological studies  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(D-; stereoselective antifibrillogenic peptides and peptidomimetics)
- IT 14133-76-7, Technetium-99, biological studies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (label; stereoselective antifibrillogenic peptides and peptidomimetics)

IT 50-99-7, Glucose, biological studies 63-91-2, Phenylalanine, biological studies

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (linker; stereoselective antifibrillogenic peptides and peptidomimetics)

IT 107761-42-2, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety)

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (stereoselective antifibrillogenic peptides and peptidomimetics)

IT 153247-40-6D, analogs 176390-09-3D, analogs 176390-19-5D, analogs 176390-21-9D, analogs 190775-14-5D, analogs 206198-57-4D, analogs 307299-71-4D, analogs 307299-72-5D, analogs 307299-73-6D, analogs 307299-74-7D, analogs 307299-75-8D, analogs 307299-76-9D, analogs 307299-77-0D, analogs 307299-78-1D, analogs

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stereoselective antifibrillogenic peptides and peptidomimetics)

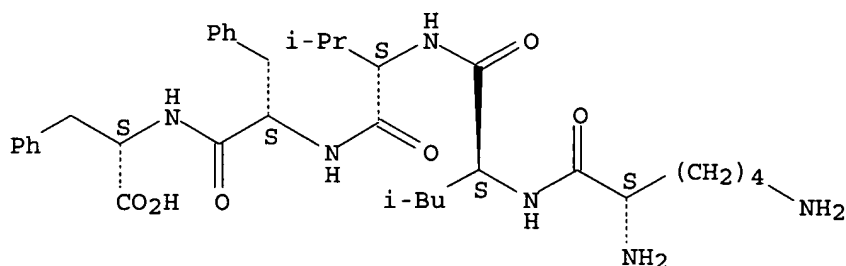
IT 153247-40-6D, analogs

RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stereoselective antifibrillogenic peptides and peptidomimetics)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 14 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2000:96000 HCAPLUS

DN 132:146648

ED Entered STN: 10 Feb 2000

TI Peptide inhibitors of  $\beta$ -amyloid toxicity

IN Kiessling, Laura L.; Murphy, Regina M.

PA Wisconsin Alumni Research Foundation, USA

SO U.S., 15 pp.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K038-00

NCL 514014000

CC 1-11 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI US 6022859 A 20000208 US 1997-970833 19971114 <--  
 PRAI US 1996-30840P P 19961115 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6022859	ICM	A61K038-00
	NCL	514014000
US 6022859	ECLA	C07K005/10B; C07K014/47A3
AB	A $\beta$ -amyloid inhibitor is disclosed which is of relevance to the treatment of Alzheimer's disease. In one embodiment, this inhibitor comprises a recognition element that interacts specifically with $\beta$ -amyloid peptide and a disrupting element that alters $\beta$ -amyloid aggregation. In a preferable form of the present invention, the inhibitor is a peptide.	
ST	beta amyloid toxicity inhibitor Alzheimer disease	
IT	Anti-Alzheimer's agents Cytotoxicity Protein sequences (peptide inhibitors of $\beta$ -amyloid toxicity)	
IT	Peptides, biological studies RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (peptide inhibitors of $\beta$ -amyloid toxicity)	
IT	Peptides, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process) (recognition; peptide inhibitors of $\beta$ -amyloid toxicity)	
IT	Amyloid RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) ( $\beta$ -; peptide inhibitors of $\beta$ -amyloid toxicity)	
IT	153247-40-6 176390-19-5 184951-41-5 184951-43-7 184951-45-9 224645-03-8 224645-04-9 224645-06-1 224645-08-3 224645-10-7 257626-11-2 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (peptide inhibitors of $\beta$ -amyloid toxicity)	
RE.CNT	9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD	
RE	(1) Anon; WO 9425043 1994 HCAPLUS (2) Anon; WO 9520973 1995 HCAPLUS (3) Anon; WO 9531210 1995 HCAPLUS (4) Anon; WO 9628471 1996 HCAPLUS (5) Dayhoff; Atlas of Protein Sequence and Structure 1972, V5, P89 (6) Ghanta, J; J Biol Chem 1996, V271(47), P29525029528 (7) Hughes; Proc Nat'l Acad Sci USA 1996, V93, P2065 HCAPLUS (8) Katz; US 5716614 1998 HCAPLUS (9) Lars, O; J Biol Chem 1996, V271(15), P8545	
IT	153247-40-6 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (peptide inhibitors of $\beta$ -amyloid toxicity)	
RN	153247-40-6 HCAPLUS	
CN	L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)	

Absolute stereochemistry.



IT 81-25-4P, Cholic acid 107761-42-2P, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) 123529-23-7P 131438-79-4P  
**153247-40-6P** 156858-22-9P 183745-73-5P 183745-74-6P  
 183745-77-9P 183745-81-5P 183745-82-6P 183745-84-8P 183745-86-0P  
 183745-88-2P 183745-90-6P 183745-92-8P 183745-94-0P 183745-96-2P  
 183745-98-4P 183746-00-1P 183746-01-2P 183746-03-4P 183746-04-5P  
 183746-05-6P 183746-07-8P 183746-08-9P 183746-09-0P 183746-10-3P  
 183746-11-4P 183746-12-5P 183746-13-6P 183746-14-7P  
**183746-15-8P 183746-16-9P 183746-17-0P**  
 183746-18-1P 183746-19-2P 183746-20-5P 183746-21-6P 183746-22-7P  
**183746-23-8P 183746-27-2P 183746-28-3P**  
**183746-30-7P 183746-31-8P** 183746-33-0P 183746-36-3P  
 183746-44-3P **183746-46-5P 183746-48-7P** 183746-98-7P  
 183746-99-8P 183747-00-4P 183906-01-6P 183906-03-8P 183906-04-9P  
 183906-05-0P 183906-07-2P 183906-09-4P 183906-10-7P 183906-12-9P  
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 232280-27-2P 232280-28-3P 232280-29-4P 232280-30-7P 232280-31-8P  
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 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (modified peptide inhibitors of amyloid  $\beta$ -peptide polymerization and stability in monkey CSF)

IT 58-85-5, Biotin 114-04-5, Neuraminic acid 1007-01-8, 2-Norbornaneacetic acid 2216-51-5, (-)-Menthhol 2321-07-5, Fluorescein 13395-35-2, 2-Iminobiotin 16294-60-3 16629-19-9, 2-Thiophenesulfonyl chloride 35404-50-3 39098-97-0, 2-Thiopheneacetyl chloride 77273-78-0, 4-Thiazolidinecarboxylic acid, 2-oxo-, (S)- 117548-22-8 161171-06-8  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (modified peptide inhibitors of amyloid  $\beta$ -peptide polymerization and stability in monkey CSF)

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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 (38) Yan, S; Nature 1996, V382, P685 HCAPLUS

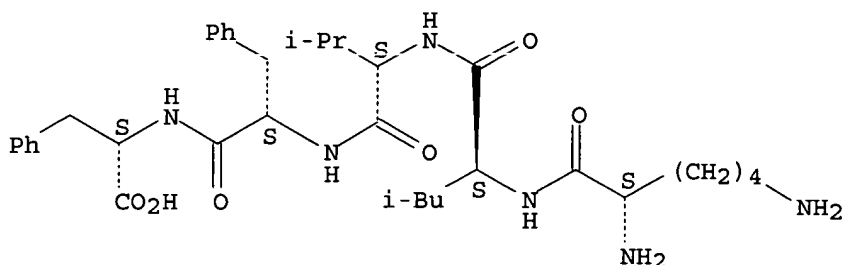
IT 153247-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (modified peptide inhibitors of amyloid  $\beta$ -peptide polymerization and stability in monkey CSF)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 16 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:166639 HCAPLUS

DN 130:209984

ED Entered STN: 15 Mar 1999

TI Synthesis of cyclosporin A conjugates for treatment of neurological disorders

IN Rich, Daniel H.; Solomon, Michael E.

PA Wisconsin Alumni Research Foundation, USA

SO PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K007-64

ICS A61K038-13

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9910374	A1	19990304	WO 1998-US17544	19980825 <--
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,  
FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,  
CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9892038 A1 19990316 AU 1998-92038 19980825 <--  
US 6316405 B1 20011113 US 1999-242724 19990222 <--  
PRAI US 1997-57751P P 19970826 <--  
WO 1998-US17544 W 19980825 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9910374	ICM	C07K007-64
	ICS	A61K038-13
WO 9910374	ECLA	C07K007/64A
OS	MARPAT 130:209984	
AB	Cyclosporin A (CsA) conjugates, cyclo(V-Abu-W-X-Val-X'-Y(Z)-D-Ala-MeLeu-MeLeu-MeVal) [V = MeLeu(3-OH), MeLeu, MeSer, MeSer-PG, MeThr, MeThr-PG, where PG is a side-chain protecting group; W = D-N-Me amino acid or N-methylglycyl residue; X, X' = N-methylleucynyl or N-methylalanyl residue; Y = lysyl, homo-lysyl, ornithinyl, lysyl-PG, homo-lysyl-PG, or ornithinyl-PG residue; Z is a polypeptide comprising 5 or more contiguous residues of Aβ peptide], were prepared for the treatment of neurol. disorders. Thus, the synthesis of Ac-EKLVFF-NH <sub>2</sub> /[MeLeu(3-OH) <sub>1</sub> , D-MeAla <sub>4,6</sub> , Lys <sub>7</sub> ]CsA conjugate is described.	
ST	cyclosporin A conjugate prepn treatment neurol disorder	
IT	Nervous system (disease; synthesis of cyclosporin A conjugates for treatment of neurol. disorders)	
IT	Peptides, preparation RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (synthesis of cyclosporin A conjugates for treatment of neurol. disorders)	
IT	78-84-2, Isobutyraldehyde 100-83-4, 3-Hydroxybenzaldehyde 107-59-5, tert-Butyl chloroacetate 598-21-0, Bromoacetyl bromide 624-83-9, Methyl isocyanate 7693-46-1, p-Nitrophenyl chloroformate 15790-86-0 26250-84-0 28276-08-6, 1,1-Dimethylpropylmagnesium chloride 59865-13-3, Cyclosporin a 90719-32-7 90878-19-6, Phenethylmagnesium chloride 220871-31-8 220903-92-4 220903-96-8 <b>220904-02-9</b> 220904-03-0 <b>220904-04-1</b> 220904-05-2 220904-06-3 <b>220904-12-1</b> 220904-13-2 RL: RCT (Reactant); RACT (Reactant or reagent) (synthesis of cyclosporin A conjugates for treatment of neurol. disorders)	
IT	69143-05-1P 76106-73-5P 82290-66-2P 83602-41-9P 89270-28-0P 124093-26-1P 129549-13-9P 138957-23-0P 152754-55-7P 152754-60-4P 152754-61-5P 152754-62-6P 152754-63-7P 177315-92-3P 178445-79-9P 178446-01-0P 178446-57-6P 220871-18-1P 220871-20-5P 220871-21-6P 220871-22-7P 220871-23-8P 220871-24-9P 220871-25-0P 220871-26-1P 220871-27-2P 220871-28-3P 220871-29-4P 220871-30-7P 220871-32-9P 220871-33-0P 220871-34-1P 220871-35-2P 220871-36-3P 220871-37-4P 220871-38-5P 220871-39-6P 220871-40-9P 220871-41-0P 220871-42-1P 220871-43-2P 220871-44-3P 220871-45-4P 220871-46-5P 220871-47-6P 220871-48-7P 220903-93-5P 220903-94-6P 220903-95-7P 220903-97-9P 220903-98-0P 220903-99-1P 220904-00-7P 220904-01-8P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (synthesis of cyclosporin A conjugates for treatment of neurol. disorders)	
IT	104324-15-4P 220871-19-2P 220871-49-8P RL: SPN (Synthetic preparation); PREP (Preparation) (synthesis of cyclosporin A conjugates for treatment of neurol. disorders)	
IT	220904-07-4P 220904-08-5P 220904-09-6P 220904-10-9P 220904-11-0P	



RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(synthesis of cyclosporin A conjugates for treatment of neurol. disorders)

RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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- (2) Edward, S; The design and synthesis of novel dual inhibitor cyclosporin A conjugates 1997, P397
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- (5) Solomon, M; 212TH AMERICAN CHEMICAL SOCIETY NATIONAL MEETING 1996
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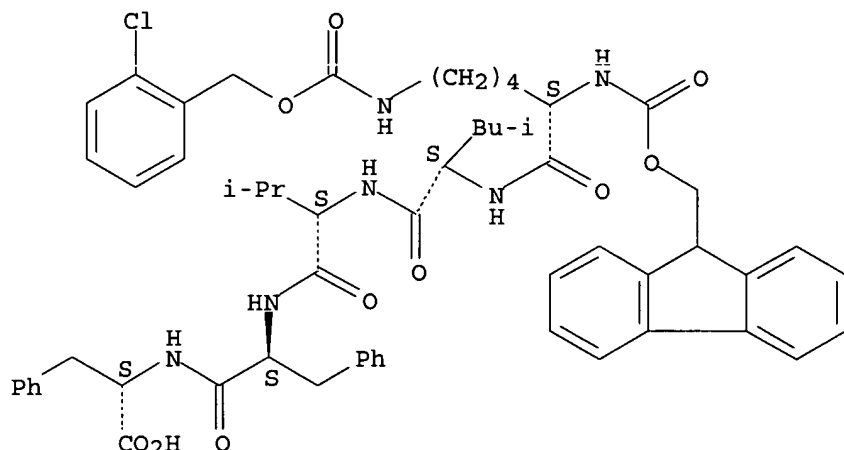
IT 220904-02-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis of cyclosporin A conjugates for treatment of neurol. disorders)

RN 220904-02-9 HCAPLUS

CN L-Phenylalanine, N6-[[[(2-chlorophenyl)methoxy]carbonyl]-N2-[(9H-fluoren-9-ylmethoxy)carbonyl]-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 17 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:148185 HCAPLUS

DN 130:347290

ED Entered STN: 09 Mar 1999

TI Recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity

AU Pallitto, Monica M.; Ghanta, Jyothi; Heinzelman, Peter; Kiessling, Laura L.; Murphy, Regina M.

CS Departments of Chemical Engineering and Chemistry, University of Wisconsin, Madison, WI, 53706, USA

SO Biochemistry (1999), 38(12), 3570-3578

CODEN: BICHAW; ISSN: 0006-2960

PB American Chemical Society

DT Journal

LA English

CC 1-11 (Pharmacology)

AB  $\beta$ -Amyloid ( $A\beta$ ), the primary protein component of Alzheimer's plaques, is neurotoxic when aggregated into fibrils. We have devised a modular strategy for generating compds. that inhibit  $A\beta$  toxicity,

based on linking a recognition element for A $\beta$  to a disrupting element designed to interfere with A $\beta$  aggregation. One such compound, with the 15-25 sequence of A $\beta$  as the recognition element and a lysine hexamer as the disrupting element, altered A $\beta$  aggregation kinetics and protected cells from A $\beta$  toxicity [Ghanta et al. (1996) J. Biol. Chemical 271, 29525]. To optimize the recognition element, peptides of 4-8 residues composed of overlapping sequences within the 15-25 domain were synthesized, along with hybrid compds. containing those recognition sequences coupled to a lysine hexamer. None of the recognition peptides altered A $\beta$  aggregation kinetics and only two, KLVFF and KLVF, had any protective effect against A $\beta$  toxicity. The hybrid peptide KLVFF-KKKKKK dramatically altered A $\beta$  aggregation kinetics and aggregate morphol. and provided significantly improved protection against A $\beta$  toxicity compared to the recognition peptide alone. In contrast, FAEDVG-KKKKKK possessed only modest inhibitory activity and had no marked effect on A $\beta$  aggregation. The scrambled sequence VLKFKF was nearly as effective a recognition domain as KLVFF, suggesting the hydrophobic characteristics of the recognition sequence are critical. None of the cytoprotective peptides prevented A $\beta$  aggregation; rather, they increased aggregate size and altered aggregate morphol. These results suggest that coupling recognition with disrupting elements is an effective generalizable strategy for the creation of A $\beta$  inhibitors. Significantly, prevention of A $\beta$  aggregation may not be required for prevention of toxicity.

ST beta amyloid aggregation inhibitor recognition peptide Alzheimer  
IT Alzheimer's disease

Cytotoxicity

Drug design

Hydrophobicity

Molecular recognition

(recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

IT Amyloid precursor proteins

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

IT Amyloid

RL: ADV (Adverse effect, including toxicity); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

( $\beta$ -; recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

( $\beta$ -amyloid inhibitors; recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

IT 153247-40-6P 176390-18-4P 176390-19-5P 184951-41-5P

184951-43-7P 224645-03-8P 224645-04-9P 224645-06-1P

224645-07-2P 224645-08-3P 224645-09-4P 224645-10-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

RE.CNT 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 153247-40-6P

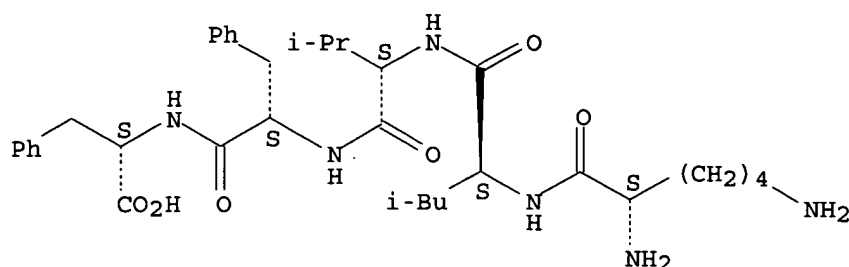
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(recognition sequence design for peptidyl modulators of  $\beta$ -amyloid aggregation and toxicity)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 18 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:21679 HCAPLUS

DN 130:95847

ED Entered STN: 12 Jan 1999

TI Preparation of amyloid  $\beta$  peptides and derivatives that modulate  $\beta$ -amyloid aggregation

IN Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; Reed, Michael; Molineaux, Susan; Kubasek, William; Chin, Joseph; Lee, Jung-Ja; Kelley, Michael

PA Praecis Pharmaceuticals, Inc., USA

SO U.S., 52 pp., Cont.-in-part of U.S. Ser. No. 404,831.

CODEN: USXXAM

DT Patent

LA English

IC ICM C07K014-435

ICS C07K007-08

NCL 514002000

CC 34-3 (Amino Acids, Peptides, and Proteins)

Section cross-reference(s): 1

FAN.CNT 7

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5854204	A	19981229	US 1996-612785	19960314 <--
	US 5817626	A	19981006	US 1995-404831	19950314 <--
	US 5854215	A	19981229	US 1995-475579	19950607 <--
	AU 759036	B2	20030403	AU 2000-35389	20000519 <--
	AU 769915	B2	20040212	AU 2002-15539	20020211 <--
PRAI	US 1995-404831	A2	19950314	<--	
	US 1995-475579	A2	19950607	<--	
	US 1995-548998	A2	19951027	<--	
	AU 1996-52524	A3	19960314	<--	
	AU 1997-42387	A3	19970827	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
US 5854204	ICM	C07K014-435	
	ICS	C07K007-08	
	NCL	514002000	
US 5854204	ECLA	C07K014/47A3	<--
US 5817626	ECLA	C07K014/47A3	<--
US 5854215	ECLA	C07K014/47A3	<--

AB Comps. that modulate the aggregation of amyloidogenic proteins or peptides are disclosed. The modulators of the invention can promote amyloid aggregation or, more preferably, can inhibit natural amyloid aggregation. In a preferred embodiment, the comps. modulate the aggregation of natural  $\beta$  amyloid peptides ( $\beta$ -AP). In a preferred embodiment, the  $\beta$  amyloid modulator comps. of the invention are comprised of an A $\beta$  aggregation core domain and a

modifying group coupled thereto such that the compound alters the aggregation or inhibits the neurotoxicity of natural  $\beta$  amyloid peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural  $\beta$ -AP aggregation when the natural  $\beta$ -APs are in a molar excess amount relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compds. of the invention, are also disclosed.

ST amyloid peptide aggregation inhibitor prepn Alzheimer treatment

IT Amyloidosis

Anti-Alzheimer's agents

(preparation of amyloid  $\beta$  peptides and derivs. that modulate  $\beta$ -amyloid aggregation)

IT Amyloid

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

( $\beta$ -; preparation of amyloid  $\beta$  peptides and derivs. that modulate  $\beta$ -amyloid aggregation)

IT 81-25-4, Cholic acid

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)

(preparation of amyloid  $\beta$  peptides and derivs. that modulate  $\beta$ -amyloid aggregation)

IT 123529-23-7P **153247-40-6P** 156858-22-9P 182912-78-3P  
 183745-73-5P 183745-74-6P 183745-77-9P 183745-79-1P 183745-81-5P  
 183745-82-6P 183745-84-8P 183745-86-0P 183745-88-2P 183745-90-6P  
 183745-92-8P 183746-04-5P 183746-05-6P 183746-07-8P 183746-08-9P  
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 183746-14-7P **183746-15-8P 183746-16-9P**  
**183746-17-0P** 183746-18-1P 183746-19-2P 183746-20-5P  
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**183746-26-1P 183746-27-2P 183746-28-3P**  
**183746-30-7P 183746-31-8P** 183746-33-0P 183746-36-3P  
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 219127-35-2P 219127-36-3P 219127-38-5P 219127-40-9P 219127-41-0P  
 219127-42-1P **219127-44-3P** 219127-49-8P **219127-50-1P**  
 219127-52-3P 219127-55-6P 219127-56-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of amyloid  $\beta$  peptides and derivs. that modulate  $\beta$ -amyloid aggregation)

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (1) Anon; EP 554887 A1 1993 HCAPLUS
- (2) Anon; WO 9304194 1993 HCAPLUS
- (3) Anon; WO 9428412 1994 HCAPLUS
- (4) Anon; EP 641861 A1 1995 HCAPLUS
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 (23) Potter; US 5338663 1994 HCAPLUS  
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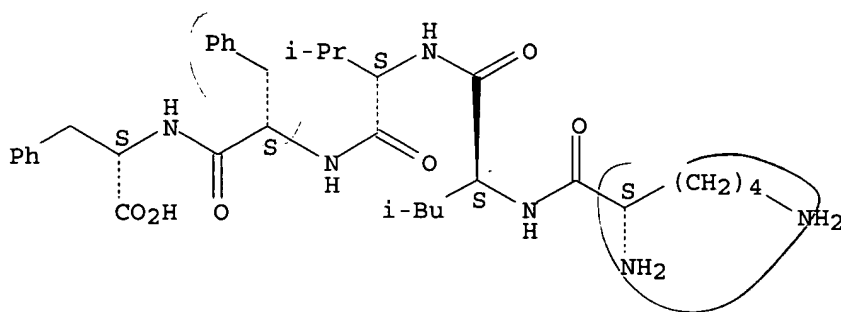
IT 153247-40-6P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of amyloid  $\beta$  peptides and derivs. that modulate  $\beta$ -amyloid aggregation)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



Lys-leu-Val-phe-phe  
 5854204  
 SEQ ID NO: 9  
 7,8,10

L45 ANSWER 19 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:197424 HCAPLUS

DN 128:266268

ED Entered STN: 06 Apr 1998

TI Identification of agents that protect against inflammatory injury to neurons

IN Giulian, Dana J.

PA Baylor College of Medicine, USA; Giulian, Dana J.

SO PCT Int. Appl., 149 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K049-00

ICS G01N031-00; G01N033-48; G01N033-53; G01N033-567; G01N033-569

CC 1-11 (Pharmacology)

Section cross-reference(s): 63

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9811923	A1	19980326	WO 1997-US16999	19970919 <--
	W: AU, CA, JP, US, US				

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE  
 US 6071493 A 20000606 US 1996-717551 19960920 <--  
 US 6043283 A 20000328 US 1997-870967 19970606 <--  
 CA 2265896 AA 19980326 CA 1997-2265896 19970919 <--  
 AU 9745894 A1 19980414 AU 1997-45894 19970919 <--  
 AU 738509 B2 20010920  
 EP 1051195 A1 20001115 EP 1997-944385 19970919 <--  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, FI  
 JP 2002504988 T2 20020212 JP 1998-514998 19970919 <--  
 PRAI US 1996-717551 A2 19960920 <--  
 US 1997-870967 A2 19970606 <--  
 WO 1997-US16999 W 19970919 <--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9811923	ICM	A61K049-00	
	ICS	G01N031-00; G01N033-48; G01N033-53; G01N033-567; G01N033-569	
WO 9811923	ECLA	A61K051/04; G01N033/50D2; G01N033/68V2	<--
US 6071493	ECLA	A61K051/04; G01N033/50D2; G01N033/68V2	<--
US 6043283	ECLA	A61K051/04; G01N033/50D2; G01N033/68V2	<--
OS	MARPAT 128:266268		
AB	Methods are disclosed for identifying agents that inhibit the toxic effects of neurotoxins on neurons from plaque component-activated mononuclear phagocytes. Also disclosed are methods for identifying agents that inhibit mononuclear phagocyte-plaque component complex formation, plaque component activation of mononuclear phagocytes, and plaque component-induced neurotoxicity of mononuclear phagocytes. The invention is also directed to agents and pharmaceutical compns. obtained by the identification methods described. Addnl., the invention describes methods for using tyramine compds. to inhibit the toxic effects of neurotoxins and methods to treat and diagnose neurodegenerative diseases and disorders.		
ST	neuron inflammatory injury neuroprotectant identification; mononuclear phagocyte plaque component neurotoxicity neuroprotection; neurodegenerative disease diagnosis therapeutic; tyramine compd neuroprotectant		
IT	Apolipoproteins RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (A; identification of agents that protect against inflammatory injury to neurons)		
IT	AIDS (disease) AIDS (disease) (AIDS dementia complex; identification of agents that protect against inflammatory injury to neurons)		
IT	Mental disorder Mental disorder (AIDS dementia; identification of agents that protect against inflammatory injury to neurons)		
IT	Brain, disease Prion diseases (Creutzfeldt-Jakob, plaque component from; identification of agents that protect against inflammatory injury to neurons)		
IT	Apolipoproteins RL: BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process) (E; identification of agents that protect against inflammatory injury to neurons)		
IT	Apolipoproteins RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)		

(Lp(a); identification of agents that protect against inflammatory injury to neurons)

IT Glutamate receptors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (NMDA-binding; identification of agents that protect against inflammatory injury to neurons)

IT mRNA  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (Scavenger receptor II; identification of agents that protect against inflammatory injury to neurons)

IT Phenols, biological studies  
 Phenols, biological studies  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (amino; identification of agents that protect against inflammatory injury to neurons)

IT Brain, disease  
 (amyloid angiopathy, plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Nervous system  
 (amyotrophic lateral sclerosis, plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Macrophage  
 (and macrophage precursor cells and macrophage-like cells; identification of agents that protect against inflammatory injury to neurons)

IT Monocyte  
 (and monocyte precursor cells and monocyte-like cells; identification of agents that protect against inflammatory injury to neurons)

IT Nucleic acids  
 RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)  
 (biosynthesis; identification of agents that protect against inflammatory injury to neurons)

IT Cat (Felis catus)  
 Dog (Canis familiaris)  
 Guinea pig (Cavia porcellus)  
 Primate  
 Rabbit  
 Rodent  
 Swine  
 (brain; identification of agents that protect against inflammatory injury to neurons)

IT Nerve, disease  
 (death; identification of agents that protect against inflammatory injury to neurons)

IT Nervous system  
 (degeneration; identification of agents that protect against inflammatory injury to neurons)

IT Amyloidosis  
 (hereditary, cerebral hemorrhage type, Dutch type, plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Brain  
 (hippocampus; identification of agents that protect against inflammatory injury to neurons)

IT Anti-Alzheimer's agents  
 Antiparkinsonian agents  
 Astrocyte  
 Brain  
 Cell morphology



Drug delivery systems  
 Drug screening  
 Nucleic acid amplification (method)  
 Structure-activity relationship  
 Translation, genetic  
     (identification of agents that protect against inflammatory injury to neurons)  
 IT Peptides, biological studies  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
     (identification of agents that protect against inflammatory injury to neurons)  
 IT Glycoproteins, general, biological studies  
     RL: BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)  
     (identification of agents that protect against inflammatory injury to neurons)  
 IT Human immunodeficiency virus 1  
     (infection; identification of agents that protect against inflammatory injury to neurons)  
 IT Signal transduction, biological  
     (inhibitors; identification of agents that protect against inflammatory injury to neurons)  
 IT Nerve, disease  
     (injury; identification of agents that protect against inflammatory injury to neurons)  
 IT Lipoproteins  
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
     (low-d., acetylated, saporin conjugates; identification of agents that protect against inflammatory injury to neurons)  
 IT Ion channel  
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
     (membrane ion gradients; identification of agents that protect against inflammatory injury to neurons)  
 IT Metabolism  
     (metabolic function loss; identification of agents that protect against inflammatory injury to neurons)  
 IT Neuroglia  
     (microglia, and microglia precursor cells and microglia-like cells; identification of agents that protect against inflammatory injury to neurons)  
 IT Respiration, animal  
     (mitochondrial; identification of agents that protect against inflammatory injury to neurons)  
 IT Liposomes  
 Microspheres  
     (mononuclear phagocyte or plaque component adhered to; identification of agents that protect against inflammatory injury to neurons)  
 IT Cytokines  
 Enzymes, biological studies  
 Lipoproteins  
 Proteins, general, biological studies  
 Radicals, biological studies  
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
     (mononuclear phagocyte release of; identification of agents that protect against inflammatory injury to neurons)  
 IT Imaging  
     (mononuclear phagocyte-plaque component complex; identification of

agents that protect against inflammatory injury to neurons)

IT Phagocyte  
(mononuclear, plaque component complex formation; identification of agents that protect against inflammatory injury to neurons)

IT Cell death  
Nerve  
(neuron; identification of agents that protect against inflammatory injury to neurons)

IT Cytoprotective agents  
(neuroprotectants; identification of agents that protect against inflammatory injury to neurons)

IT Toxicity  
(neurotoxicity; identification of agents that protect against inflammatory injury to neurons)

IT Toxins  
RL: ADV (Adverse effect, including toxicity); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)  
(neurotoxins; identification of agents that protect against inflammatory injury to neurons)

IT Dyes  
(penetration; identification of agents that protect against inflammatory injury to neurons)

IT Amines, biological studies  
Amines, biological studies  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(phenolic; identification of agents that protect against inflammatory injury to neurons)

IT Human immunodeficiency virus  
(plaque component from infection with; identification of agents that protect against inflammatory injury to neurons)

IT Alzheimer's disease  
Down's syndrome  
Multiple sclerosis  
Parkinson's disease  
(plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Proteins, specific or class  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)  
(plaque; identification of agents that protect against inflammatory injury to neurons)

IT Mitochondria  
(respiration; identification of agents that protect against inflammatory injury to neurons)

IT Proteins, specific or class  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(saporins, conjugates, with acetylated LDL; identification of agents that protect against inflammatory injury to neurons)

IT Brain, disease  
(senile plaque; identification of agents that protect against inflammatory injury to neurons)

IT Brain, disease  
(spongiform encephalopathy, plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Brain, disease  
(stroke, plaque component from; identification of agents that protect against inflammatory injury to neurons)

IT Antigens  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(surface; identification of agents that protect against inflammatory

- injury to neurons)
- IT Nerve  
(toxicity; identification of agents that protect against inflammatory injury to neurons)
- IT Injury  
(trauma, plaque component from; identification of agents that protect against inflammatory injury to neurons)
- IT Scavenger receptors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(type II; identification of agents that protect against inflammatory injury to neurons)
- IT Drug delivery systems  
(unit doses; identification of agents that protect against inflammatory injury to neurons)
- IT Amyloid  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
( $\beta$ -; identification of agents that protect against inflammatory injury to neurons)
- IT 89-00-9, Quinolinic acid 77006-27-0  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(identification of agents that protect against inflammatory injury to neurons)
- IT 107015-83-8 107761-42-2, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) 107761-42-2D, Glycopeptide (human clone 9-110 amyloid A4 peptide moiety), modified 109770-29-8, 1-28-Glycopeptide (human clone 9-110 amyloid A4 peptide moiety) 118427-80-8 131438-79-4 131580-10-4 131602-53-4 133605-53-5 144409-98-3 146621-55-8 152286-31-2 155178-13-5D, carboxyl-terminal variants 176390-02-6 176390-21-9 190436-05-6 205437-69-0 205437-73-6 205454-00-8  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(identification of agents that protect against inflammatory injury to neurons)
- IT 50-02-2, Dexamethasone 51-61-6, Dopamine, biological studies 51-67-2, Tyramine 51-67-2D, Tyramine, derivs. 53-86-1, Indomethacin 54-05-7, Chloroquine 54-05-7D, Chloroquine, derivs. 60-18-4, Tyrosine, biological studies 64-86-8, Colchicine 70-18-8, Glutathione, biological studies 104-14-3, Octopamine 145-63-1, Suramine 446-72-0, Genistein 477-84-9, Damnacanthal 556-02-5, D-Tyrosine 949-67-7, L-Tyrosine ethyl ester 1080-06-4, L-Tyrosine methyl ester 1406-18-4, Vitamin E 4357-95-3, L-Tyrosine  $\beta$ -naphthylamide 6292-90-6, L-Tyrosine butyl ester 6384-92-5, NMDA 7662-51-3, L-Tyrosine hydrazide 9001-05-2, Catalase 10182-84-0, Diphenyl iodonium 16874-12-7, L-Tyrosine tert-butyl ester 16874-12-7D, Tyrosine tert-butyl ester, mono- and di-iodinated 23210-56-2, Ifenprodil 42406-77-9, L-Tyrosine benzyl ester 76326-31-3, AP5 77086-22-7, MK801 85797-13-3, AP7 90237-02-8, GAMS 118876-58-7 125441-04-5, L-Tyrosine allyl ester 125441-05-6 150403-88-6 154447-36-6, LY294002  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(identification of agents that protect against inflammatory injury to neurons)
- IT 9001-92-7, Protease 9005-49-6, Heparin sulfate, biological studies 9050-30-0, Heparan sulfate  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(identification of agents that protect against inflammatory injury to neurons)
- IT 141176-92-3P  
RL: PUR (Purification or recovery); PREP (Preparation)

(identification of agents that protect against inflammatory injury to neurons)

IT 72-57-1, Trypan blue  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(identification of agents that protect against inflammatory injury to neurons)

IT 80449-02-1, Tyrosine kinase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(inhibitors; identification of agents that protect against inflammatory injury to neurons)

IT 50-99-7, Glucose, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(metabolism; identification of agents that protect against inflammatory injury to neurons)

IT 9012-36-6, Sepharose 9014-76-0, Sephadex  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(mononuclear phagocyte or plaque component adhered to; identification of agents that protect against inflammatory injury to neurons)

IT 10102-43-9, Nitric oxide, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(mononuclear phagocyte release of; identification of agents that protect against inflammatory injury to neurons)

IT 56-65-5, Adenosine triphosphate, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)  
(production; identification of agents that protect against inflammatory injury to neurons)

IT 141256-43-1, Antichymotrypsin  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
( $\alpha$ -; identification of agents that protect against inflammatory injury to neurons)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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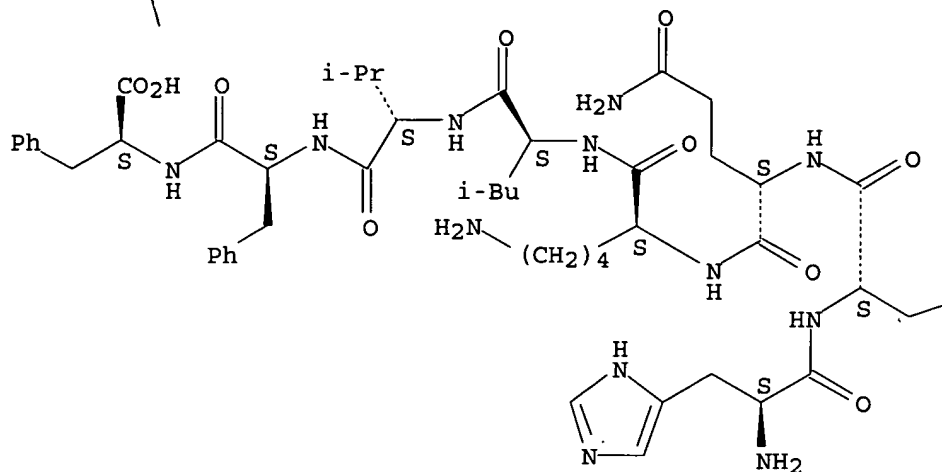
IT 176390-02-6  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(identification of agents that protect against inflammatory injury to neurons)

RN 176390-02-6 HCAPLUS

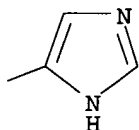
CN L-Phenylalanine, L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L45 ANSWER 20 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:137096 HCAPLUS

DN 128:305262

ED Entered STN: 09 Mar 1998

TI Measurement of peptide aggregation with pulsed-field gradient nuclear magnetic resonance spectroscopy

AU Mansfield, Shawn L.; Jayawickrama, Dimuthu A.; Timmons, Jeffery S.; Larive, Cynthia K.

CS Department of Chemistry, University of Kansas, Lawrence, KS, 66045, USA

SO Biochimica et Biophysica Acta (1998), 1382(2), 257-265

CODEN: BBACAQ; ISSN: 0006-3002

PB Elsevier Science B.V.

DT Journal

LA English

CC 6-3 (General Biochemistry)

AB Interactions between hydrophobic patches in proteins are often a driving force for denaturation and aggregation. The aggregation of the  $\beta$ -amyloid peptide fragment, VHHQKLVFFAEDVGSNK ( $\beta$ (12-28)), has been investigated in aqueous solution at low pH. This peptide contains a central

hydrophobic patch spanning residues 17-21. Diffusion coeffs. measured with pulsed-field gradient NMR as a function of peptide solution concentration were

used to assess the extent of aggregation. Following the hypothesis that hydrophobic interactions are an important driving force in the aggregation of this peptide at low pH, a non-aggregating analog of the  $\beta(12-28)$  peptide, [Gly19,20] $\beta(12-28)$  was synthesized. In the [Gly19,20] $\beta(12-28)$  peptide, the replacement of the two phenylalanine residues disrupts the hydrophobic interactions which drive the aggregation of  $\beta(12-28)$ . The diffusion coefficient of the [Gly19,20] $\beta(12-28)$  peptide is invariant over the concentration range studied and provides a good estimate of the monomeric diffusion coefficient of  $\beta(12-28)$ . A second peptide analog was synthesized in which the phenylalanine at position 20 was replaced with a cysteine residue. The disulfide-linked dimer, ([Cys20] $\beta(12-28)$ )<sub>2</sub>, was formed upon air oxidation of this peptide. The diffusion coefficient of the ([Cys20] $\beta(12-28)$ )<sub>2</sub> peptide was measured and used to estimate the diffusion coefficient of the  $\beta(12-28)$  dimer. Using the monomeric and dimeric diffusion coeffs. measured for the glycine and cysteine analogs, the concentration dependence of the  $\beta(12-28)$  diffusion coefficient was found to be consistent with a monomer-dimer aggregation model.

ST beta amyloid peptide aggregation monomer dimer

IT Aggregation

Diffusion

Hydrophobicity

Self-association

( $\beta$ -amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy)

IT Peptides, biological studies

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

( $\beta$ -amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy)

IT 107015-83-8

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

( $\beta$ -amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy)

IT 206198-56-3P 206198-57-4P 206281-19-8P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

( $\beta$ -amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy)

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 206198-57-4P

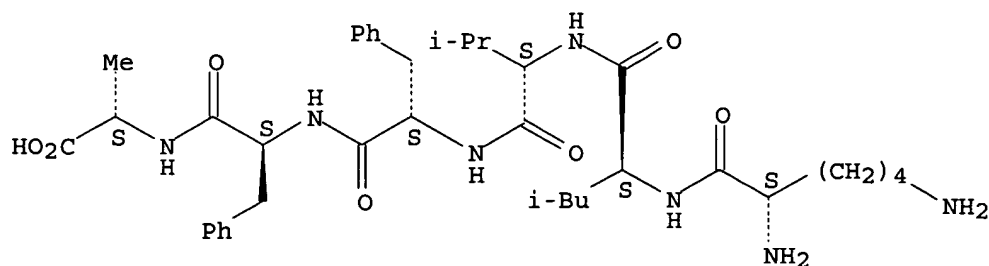
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

( $\beta$ -amyloid peptide and analogs monomer-dimer aggregation studied by pulsed-field gradient NMR spectroscopy)

RN 206198-57-4 HCAPLUS

CN L-Alanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl-L-phenylalanyl- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



DN 127:117394  
 ED Entered STN: 14 Aug 1997  
 TI Peptide binding the KLVFF sequence of amyloid  $\beta$   
 IN Nordstedt, Christer; Naslund, Jan; Thyberg, Johan; Tjernberg, Lars O.;  
 Terenius, Lars  
 PA Karolinska Innovations Ab, Swed.; Nordstedt, Christer; Naslund, Jan;  
 Thyberg, Johan; Tjernberg, Lars O.; Terenius, Lars  
 SO PCT Int. Appl., 30 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-47  
 ICS C07K007-04  
 CC 1-11 (Pharmacology)  
 Section cross-reference(s): 14, 34

## FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9721728	A1	19970619	WO 1996-SE1621	19961209 <--
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, VZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	AU 9710728	A1	19970703	AU 1997-10728	19961209 <--
	EP 866805	A1	19980930	EP 1996-940740	19961209 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6331440	B1	20011218	US 1998-95106	19980610 <--
	US 2002094957	A1	20020718	US 2001-850061	20010508 <--
	US 2004157781	A1	20040812	US 2003-721774	20031126 <--
PRAI	SE 1995-4467	A	19951212	<--	
	US 1995-9386P	P	19951229	<--	
	WO 1996-SE1621	W	19961209	<--	
	US 1998-95106	A3	19980610	<--	
	US 2001-850061	A1	20010508		

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9721728	ICM	C07K014-47
	ICS	C07K007-04
WO 9721728	ECLA	C07K005/08A1B; C07K005/08B; C07K005/08C; C07K005/08H1; C07K005/10A1B; C07K005/10B; C07K005/10C; C07K005/10H; C07K014/47A3; G01N033/68V2 <--
US 6331440	ECLA	C07K014/47A3; G01N033/68V2 <--
US 2002094957	ECLA	C07K005/08A1B; C07K005/08B; C07K005/08C; C07K005/08H1; C07K005/10A1B; C07K005/10B; C07K005/10C; C07K005/10H; C07K014/47A3; G01N033/68V2 <--
US 2004157781	ECLA	C07K005/08A1B; C07K005/08B; C07K005/08C; C07K005/08H1; C07K005/10A1B; C07K005/10B; C07K005/10C; C07K005/10H; C07K014/47A3; G01N033/68V2 <--

AB The invention relates to compds. of formula which are of interest especially for

inhibition of polymerization of amyloid  $\beta$  peptide, as model substances for synthesis of amyloid  $\beta$  peptide-ligands, as tool for the identification of other organic compds. with similar functional properties and/or as ligands for detection of amyloid deposits using E.G. positron emission topog. (PET). KLVFF, an amyloid  $\beta$  sequence, was identified and was shown to be required for amyloid fibril formation. Ligands binding to KLVFF may inhibit fibril formation and could be of therapeutic



value in treatment of Alzheimer's disease.

ST beta amyloid polymn KLVFF sequence inhibitor

IT Alzheimer's disease  
(peptide binding the KLVFF sequence of amyloid  $\beta$  and inhibition of amyloid polymerization)

IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(peptide binding the KLVFF sequence of amyloid  $\beta$  and inhibition of amyloid polymerization)

IT Amyloid  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
( $\beta$ -; peptide binding the KLVFF sequence of amyloid  $\beta$  and inhibition of amyloid polymerization)

IT 64533-15-9P 134649-29-9P 138647-36-6P 141684-15-3P  
152647-23-9P 153247-40-6P 176390-00-4P  
176390-01-5P 176390-02-6P 176390-03-7P  
176390-04-8P 176390-05-9P 176390-06-0P 176390-07-1P  
176390-08-2P 176390-09-3P 176390-10-6P 176390-11-7P  
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176390-16-2P 176390-17-3P 176390-18-4P 176390-19-5P  
176390-20-8P 176390-21-9P 176390-22-0P 176390-23-1P 176390-24-2P  
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RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(peptide binding the KLVFF sequence of amyloid  $\beta$  and inhibition of amyloid polymerization)

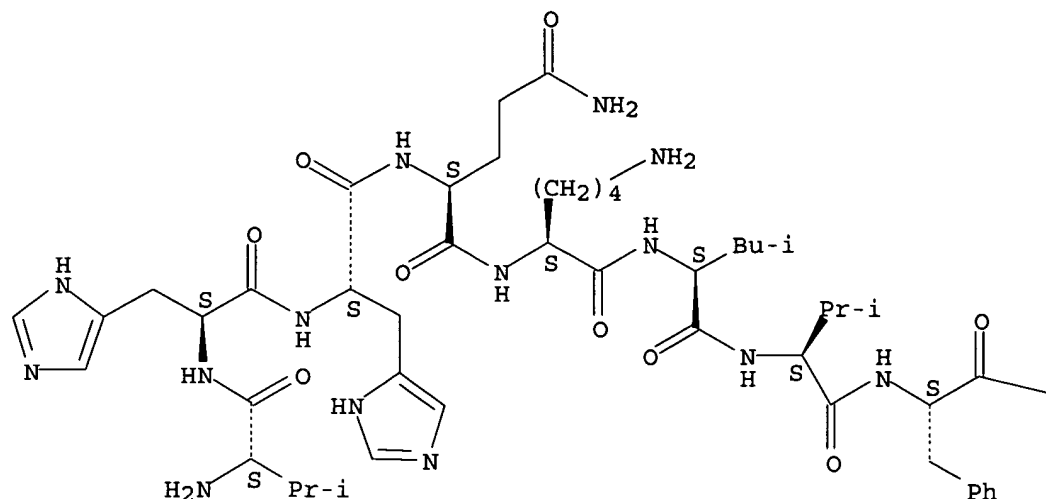
IT 134649-29-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(peptide binding the KLVFF sequence of amyloid  $\beta$  and inhibition of amyloid polymerization)

RN 134649-29-9 HCAPLUS

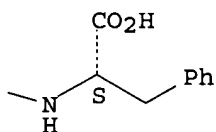
CN L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminy-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L45 ANSWER 22 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1997:458252 HCAPLUS  
 DN 127:107496  
 ED Entered STN: 23 Jul 1997  
 TI Controlling amyloid  $\beta$ -peptide fibril formation with protease-stable  
 ligands. [Erratum to document cited in CA127:32334]  
 AU Tjernberg, Lars O.; Lilliehook, Christina; Callaway, David J. E.; Naslund,  
 Jan; Hahne, Solveig; Thyberg, Johan; Terenius, Lars; Nordstedt, Christer  
 CS Lab. Biochem. Mol. Pharmacol., Sect. Drug Dependence Res., Dep. Clinical  
 Neurosci., Karolinska Hosp., Stockholm, S-171 76, Swed.  
 SO Journal of Biological Chemistry (1997), 272(28), 17894  
 CODEN: JBCHA3; ISSN: 0021-9258  
 PB American Society for Biochemistry and Molecular Biology  
 DT Journal  
 LA English  
 CC 14-10 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 1  
 AB The micrograph in Fig. 5 did not reproduce adequately. Fig. 5 is

reproduced in better quality.

ST erratum Alzheimer amyloid fibril peptide ligand; Alzheimer amyloid fibril peptide ligand erratum

IT Combinatorial library  
Molecular association  
Molecular modeling  
Protein motifs  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation (Erratum))

IT Peptidomimetics  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation in relation to (Erratum))

IT Structure-activity relationship  
(amyloid peptide-binding; of peptide homologs (Erratum))

IT Organelle  
(fibril; D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation (Erratum))

IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(pentapeptides; D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation (Erratum))

IT 131438-79-4  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation (Erratum))

IT 190775-15-6 190775-16-7 190775-17-8 190775-18-9 190775-19-0  
190775-20-3 190775-21-4 190775-22-5 190775-23-6 190775-24-7  
190775-25-8 190775-26-9 190775-27-0 190775-28-1 190775-29-2  
190775-30-5 190775-31-6 190775-32-7 190775-33-8 190775-34-9  
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190775-40-7 190775-41-8 190775-42-9 190775-43-0 190775-44-1  
190775-45-2 190775-46-3 190775-47-4 190775-48-5 190775-49-6  
190775-50-9 190775-51-0 190775-52-1 190775-53-2  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation (Erratum))

IT 190775-13-4  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(peptide homolog association with (Erratum))

IT 153247-40-6D, peptides-containing  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
( $\beta$ -amyloid peptide association with (Erratum))

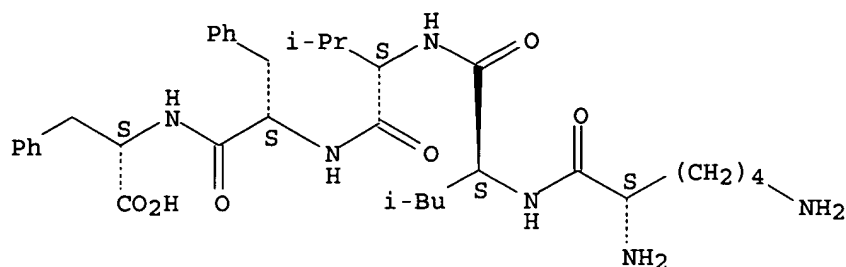
IT 190775-14-5  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
( $\beta$ -amyloid peptide association with (Erratum))

IT 153247-40-6D, peptides-containing  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
( $\beta$ -amyloid peptide association with (Erratum))

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 23 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:318416 HCAPLUS

DN 127:32334

ED Entered STN: 19 May 1997

TI Controlling amyloid  $\beta$ -peptide fibril formation with protease-stable ligands

AU Tjerenberg, Lars O.; Lilliehook, Christina; Callawya, David J. E.; Naslund, Jan; Hahne, Solveig; Thyberg, Johan; Terenius, Lars; Nordstedt, Christer

CS Lab. Biochem. Mol. Pharmacol., Sect. Drug Dependence Res., Dep. Clinical Neurosci., Karolinska Hosp., Stockholm, S-171 76, Swed.

SO Journal of Biological Chemistry (1997), 272(19), 12601-12605  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 14-10 (Mammalian Pathological Biochemistry)

Section cross-reference(s): 1

AB The authors have previously shown that short peptides incorporating the sequence KLVFF can bind to the ~40-amino acid residue Alzheimer amyloid  $\beta$ -peptide ( $A\beta$ ) and disrupt amyloid fibril formation. Here, it is shown that KLVFF binds stereospecifically to the homologous sequence in  $A\beta$  (i.e.  $A\beta$ 16-20). Mol. modeling suggests that association of the two homologous sequences leads to the formation of an atypical anti-parallel  $\beta$ -sheet structure stabilized primarily by interaction between the Lys, Leu, and C-terminal Phe. By screening combinatorial pentapeptide libraries exclusively composed of D-amino acids, several ligands with a general motif containing phenylalanine in the second position and leucine in the third position were identified. Ligands composed of D-amino acids were not only capable of binding  $A\beta$  but also prevented formation of amyloid-like fibrils. These ligands are protease-resistant and may thus be useful as exptl. agents against amyloid fibril formation in vivo.

ST Alzheimer amyloid fibril peptide ligand

IT Structure-activity relationship  
(amyloid peptide-binding; of peptide homologs)

IT Organelle  
(fibril; D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(pentapeptides; D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

IT Combinatorial library  
Molecular association  
Molecular modeling  
Protein motifs

(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

IT Peptidomimetics  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation in relation to)

IT 190775-13-4  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(peptide homolog association with)

IT 153247-40-6D, peptides-containing  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
( $\beta$ -amyloid peptide association with)

IT 190775-14-5  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
( $\beta$ -amyloid peptide association with)

IT 131438-79-4  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

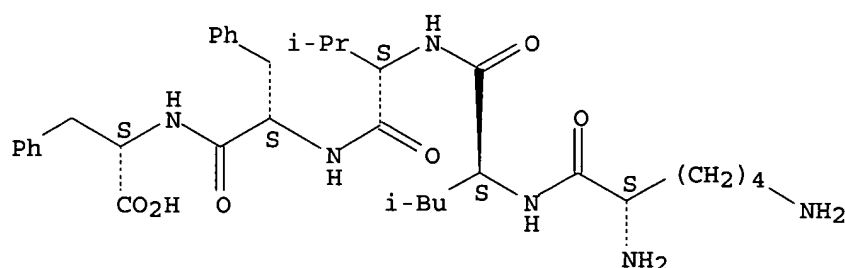
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190775-20-3 190775-21-4 190775-22-5 190775-23-6 190775-24-7  
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190775-50-9 190775-51-0 190775-52-1 190775-53-2  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(D-pentapeptides effect on  $\beta$ -amyloid peptide fibril formation)

RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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 IT 153247-40-6D, peptides-containing  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
 (β-amyloid peptide association with)  
 RN 153247-40-6 HCAPLUS  
 CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 24 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1996:748345 HCAPLUS  
 DN 126:19332  
 ED Entered STN: 21 Dec 1996  
 TI Preparation of peptides as modulators of amyloid aggregation  
 IN Findeis, Mark A.; Benjamin, Howard; Garnick, Marc B.; Gefter, Malcolm L.; Hundal, Arvind; Kasman, Laura; Musso, Gary; Signer, Ethan R.; Wakefield, James; et al.  
 PA Pharmaceutical Peptides Incorporated, USA  
 SO PCT Int. Appl., 105 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K014-47  
 ICS A61K038-17  
 CC 34-3 (Amino Acids, Peptides, and Proteins)  
 Section cross-reference(s): 1  
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9628471	A1	19960919	WO 1996-US3492	19960314 <--
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5817626	A	19981006	US 1995-404831	19950314 <--
US 5854215	A	19981229	US 1995-475579	19950607 <--
AU 9652524	A1	19961002	AU 1996-52524	19960314 <--
EP 815134	A1	19980107	EP 1996-908805	19960314 <--
EP 815134	B1	20020605		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
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AT 218583	E	20020615	AT 1996-908805	19960314 <--
AU 759036	B2	20030403	AU 2000-35389	20000519 <--
AU 769915	B2	20040212	AU 2002-15539	20020211 <--

PRAI US 1995-404831	A	19950314	<--
US 1995-475579	A	19950607	<--
US 1995-548998	A	19951027	<--
AU 1996-52524	A3	19960314	<--
WO 1996-US3492	W	19960314	<--
AU 1997-42387	A3	19970827	<--

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9628471	ICM	C07K014-47	
	ICS	A61K038-17	
WO 9628471	ECLA	C07K014/47A3	<--
US 5817626	ECLA	C07K014/47A3	<--
US 5854215	ECLA	C07K014/47A3	<--
AB	<p>Compds. that modulate the aggregation of amyloidogenic proteins or peptides are disclosed. The modulators of the invention can promote amyloid aggregation or, more preferably, can inhibit natural amyloid aggregation. In a preferred embodiment, the compds. modulate the aggregation of natural <math>\beta</math> amyloid peptides (<math>\beta</math>-AP). In a preferred embodiment, the <math>\beta</math> amyloid modulator compds. of the invention are comprised of an A<math>\beta</math> aggregation core domain and a modifying group coupled thereto such that the compound alters the aggregation or inhibits the neurotoxicity of natural <math>\beta</math> amyloid peptides when contacted with the peptides. Furthermore, the modulators are capable of altering natural <math>\beta</math>-AP aggregation when the natural <math>\beta</math>-APs are in a molar excess amount relative to the modulators. Pharmaceutical compns. comprising the compds. of the invention, and diagnostic and treatment methods for amyloidogenic diseases using the compds. of the invention, are also disclosed. These peptide compds. are bound to natural <math>\beta</math>-amyloid peptides to facilitate diagnosis of a <math>\beta</math>-amyloidogenic disease, in particular Alzheimer's disease, and are useful for treating a disorder associated with amyloidosis including, e.g. familial amyloid polyneuropathy or cardiomyopathy, isolated cardiac amyloid, systemic senile amyloidosis, scrapie, bovine spongiform encephalopathy, and Creutzfeldt-Jakob disease. Thus, N-biotinyl-DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV-OH (N-biotinyl-<math>\beta</math>-AP1-40), prepared by the solid phase synthesis using a N<math>\alpha</math>-Fmoc-based protection strategy and Fmoc-Val-Wang resin, at 1% markedly inhibited aggregation of the natural <math>\beta</math>-amyloid peptide (<math>\beta</math>-AP1-40).</p>		
ST	<p>peptide prepn modulator amyloid aggregation; diagnosis amyloidogenic disease Alzheimer disease; amyloidosis assocd disorder; familial amyloid polyneuropathy cardiomyopathy treatment peptide; isolated cardiac amyloid treatment peptide; systemic senile amyloidosis treatment peptide; scrapie treatment peptide; bovine spongiform encephalopathy treatment peptide; Creutzfeldt Jakob disease treatment peptide</p>		
IT	<p>Brain, disease Prion diseases (Creutzfeldt-Jakob; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)</p>		
IT	<p>Deafness Urticaria (Muckle-Wells syndrome in familial Mediterranean Fever and familial amyloid nephropathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)</p>		
IT	<p>Diagnosis (agents, for Alzheimer's disease; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)</p>		
IT	<p>Heart, disease Heart, disease (amyloidosis, isolated; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)</p>		
IT	<p>Nervous system</p>		

- (disease, Gerstmann-Straussler syndrome; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Amyloidosis  
Amyloidosis  
(familial Mediterranean fever, with Muckle-Wells syndrome; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Fever and Hyperthermia  
Fever and Hyperthermia  
(familial Mediterranean, with Muckle-Wells syndrome; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Kidney, disease  
(familial amyloid nephropathy with Muckle-Wells syndrome and fibrinogen-associated hereditary renal amyloidosis; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Heart, disease  
(familial amyloidotic cardiomyopathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Amyloidosis  
(familial amyloidotic polyneuropathy, type IV; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Amyloidosis  
(familial amyloidotic polyneuropathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Dialysis  
(hemodialysis, amyloidosis associated with long term hemodialysis; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Brain, disease  
(hemorrhage, hereditary cerebral hemorrhage with amyloidosis of Iceland type; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Amyloidosis  
(hereditary, lysozyme-associated; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Pancreatic islet of Langerhans  
(insulinoma; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Carcinoma  
(medullary, amyloidosis associated with thyroid medullary carcinoma; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Macroglobulins  
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)  
(metabolic disorders, macroglobulinemia, myeloma or macroglobulinemia-associated amyloidosis; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Multiple myeloma  
(myeloma or macroglobulinemia-associated amyloidosis; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)
- IT Diabetes mellitus  
(non-insulin-dependent; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)



IT Nerve, disease  
(polyneuropathy, familial amyloid; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Peptides, preparation  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloid  
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PREP (Preparation)  
(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Sjogren's syndrome  
(primary localized cutaneous nodular amyloidosis-associated; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis  
(primary; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Brain, disease  
Prion diseases  
(scrapie; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis  
(secondary; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Amyloidosis  
(senile, systemic; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Brain, disease  
(spongiform encephalopathy; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT Alzheimer's disease  
(treatment and diagnosis; preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT 123529-23-7P **153247-40-6P** 156858-22-9P 182912-78-3P  
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183906-12-9P 183906-14-1P 184051-28-3P 184051-29-4P 184051-30-7P  
184051-31-8P 184051-32-9P 184051-33-0P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT 58-85-5, Biotin 64-19-7, Acetic acid, reactions 67-43-6 81-25-4, Cholic acid 40248-63-3, (-)-Menthoxycetic acid 68858-20-8D, Wang resin-bound 72088-94-9 131438-79-4 183745-73-5 183745-81-5 183745-82-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

IT 153247-40-6P

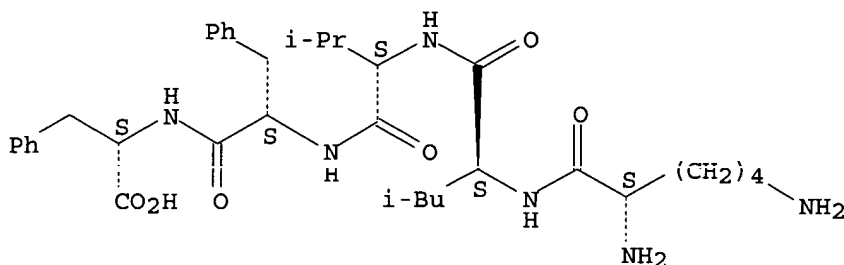
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptides as modulators of amyloid aggregation for treating amyloidosis-associated disorders)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 25 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1996:233397 HCAPLUS

DN 124:306542

ED Entered STN: 20 Apr 1996

TI Arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand

AU Tjernberg, Lars O.; Naeslund, Jan; Lindqvist, Fredrik; Johansson, Jan; Karlstroem, Anders R.; Thyberg, Johan; Terenius, Lars; Nordstedt, Christer  
CS Laboratory Biochemistry Molecular Pharmacology, Karolinska Hospital, Stockholm, S-171 76, Swed.

SO Journal of Biological Chemistry (1996), 271(15), 8545-8  
CODEN: JBCHA3; ISSN: 0021-9258

PB American Society for Biochemistry and Molecular Biology

DT Journal

LA English

CC 1-3 (Pharmacology)

AB Polymerization of amyloid  $\beta$ -peptide ( $A\beta$ ) into amyloid fibrils is a critical step in the pathogenesis of Alzheimer's disease. Here, we show that peptides incorporating a short  $A\beta$  fragment (KLVFF;  $A\beta$ 16-20) can bind full-length  $A\beta$  and prevent its assembly into amyloid fibrils. Through alanine substitution, it was demonstrated that amino acids Lys16, Leu17, and Phe20 are critical for binding to  $A\beta$  and inhibition of  $A\beta$  fibril formation. A mutant  $A\beta$  mol., in which these residues had been substituted, had a markedly reduced capability of forming amyloid fibrils. The present data suggest that residues  $A\beta$ 16-20 serve as a binding sequence during  $A\beta$  polymerization and fibril formation. Moreover, the present KLVFF peptide may serve as a lead compound for the development of peptide and nonpeptide agents aimed at inhibiting  $A\beta$  amyloidogenesis in vivo.

ST pentapeptide amyloidogenesis inhibitor Alzheimer disease

IT Molecular structure-biological activity relationship  
(amyloidogenesis-inhibiting; arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand)

IT Peptides, biological studies  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
(arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand)

IT Mental disorder  
(Alzheimer's disease, arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand)

IT Proteins, specific or class  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(amyloid A4, arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand)

IT 64533-15-9 **134649-29-9** 138647-36-6 141684-15-3 152647-23-9  
**153247-40-6 176390-00-4 176390-01-5**  
 176390-02-6 176390-03-7 176390-04-8  
 176390-05-9 176390-06-0 176390-07-1 176390-08-2  
 176390-09-3 176390-10-6 176390-11-7 176390-12-8  
 176390-13-9 176390-14-0 176390-15-1 176390-16-2  
 176390-17-3 176390-18-4 **176390-19-5** 176390-20-8  
 176390-21-9 176390-22-0 176390-23-1 176390-24-2 176390-25-3  
 176390-26-4 176390-27-5 176390-28-6 176390-29-7  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand)

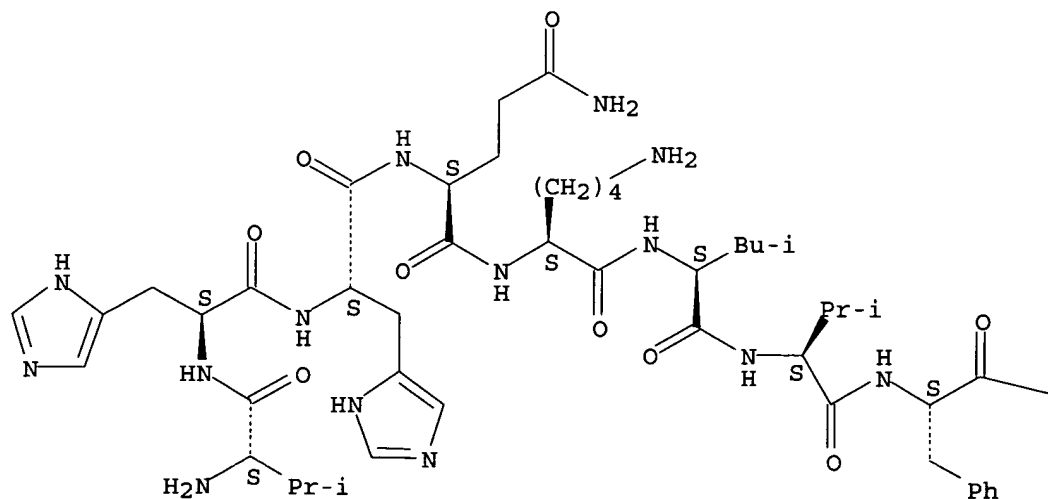
IT **134649-29-9**  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (arrest of  $\beta$ -amyloid fibril formation by a pentapeptide ligand)

RN 134649-29-9 HCAPLUS

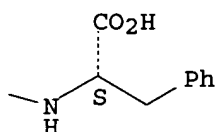
CN L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



L45 ANSWER 26 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1995:594478 HCAPLUS  
 DN 123:977  
 ED Entered STN: 08 Jun 1995  
 TI Peptides for amelioration of amnesia in Alzheimer's disease caused by  
 deposition of amyloid beta protein  
 IN Roberts, Eugene  
 PA City of Hope, USA  
 SO PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K038-00  
 ICS C07K005-00; C07K007-00; C07K017-00  
 CC 1-11 (Pharmacology)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9508999	A1	19950406	WO 1994-US10475	19940916 <--
	W: CA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5470951	A	19951128	US 1993-127904	19930929 <--
	CA 2149627	AA	19950406	CA 1994-2149627	19940916 <--
	EP 670731	A1	19950913	EP 1994-929818	19940916 <--
	R: DE, FR, GB				
PRAI	US 1993-127904	A	19930929	<--	
	WO 1994-US10475	W	19940916	<--	

## CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES	
WO 9508999	ICM	A61K038-00	
	ICS	C07K005-00; C07K007-00; C07K017-00	
WO 9508999	ECLA	C07K005/10A1A; C07K005/10C; C07K014/47A3	<--
US 5470951	ECLA	C07K005/10A1A; C07K005/10C; C07K014/47A3	<--

OS MARPAT 123:977

AB Three non-amnestic and non-memory enhancing peptides, Asp-Phe-Phe-Val-Gly, Gln-Phe-Val-Gly, and Ala-Ile-Phe-Thr, that block the amnestic effects of  $\beta$ -(12-28), a peptide homologs to amyloid  $\beta$  protein ( $A\beta$ ), are disclosed. The invention relates to amelioration of amnesia and other neurotoxicity in Alzheimer's disease (AD) caused by deposition of  $A\beta$  and, therefore, relates to attenuation of the disease process and consequential improvement of the quality of life for the individuals

suffering from AD. The effects of a series of peptides on the amnestic effects of  $\beta(12-28)$  in mice were determined

ST Alzheimer disease amnesia treatment peptide

IT Amnesia  
(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT Peptides, biological studies  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT Mental disorder  
(Alzheimer's disease, peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT Proteins, specific or class  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(amyloid A4, peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT 2131-06-8 2577-40-4, Phenylalanyl phenylalanine 3918-94-3, Valyl valine 53932-31-3 64533-12-6 140941-10-2 **153247-40-6**  
153247-41-7 153247-43-9 153247-49-5 153247-51-9 163623-31-2  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

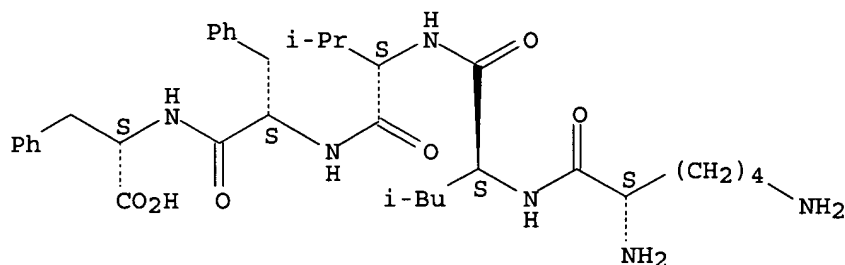
IT 153247-44-0 153247-44-0D, esters and amides 153247-48-4  
153247-48-4D, esters and amides 153247-50-8 153247-50-8D, esters and amides  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

IT **153247-40-6**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(peptides for amelioration of amnesia in Alzheimer's disease caused by deposition of amyloid  $\beta$  protein)

RN 153247-40-6 HCAPLUS

CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L45 ANSWER 27 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1995:573971 HCAPLUS

DN 122:306561

ED Entered STN: 26 May 1995

TI Use of a topographic receptor model to identify the binding site for amnestic peptides and the design of memory-enhancing drugs

IN Roberts, Eugene

PA City of Hope, USA

SO PCT Int. Appl., 50 pp.

CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K038-00  
 ICS C07K005-00; C07K005-08; C07K005-10  
 CC 1-11 (Pharmacology)  
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9507093	A1	19950316	WO 1994-US10083	19940908 <--
	W: CA, US				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5652334	A	19970729	US 1993-117927	19930908 <--
	CA 2148452	AA	19950315	CA 1994-2148452	19940908 <--
	EP 668776	A1	19950830	EP 1994-928038	19940908 <--
	EP 668776	B1	20000412		
	R: DE, FR, GB				
PRAI	US 1993-117927	A	19930908	<--	
	WO 1994-US10083	W	19940908	<--	

## CLASS

	PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
	WO 9507093	ICM	A61K038-00
		ICS	C07K005-00; C07K005-08; C07K005-10
	WO 9507093	ECLA	C07K005/02A; C07K005/02B; C07K005/02C; C07K005/10B <--
	US 5652334	ECLA	C07K005/02A; C07K005/02B; C07K005/02C; C07K005/10B <--
AB	A topog. model useful to design and synthesize memory-enhancing substances is disclosed. Administration of substances designed by this method to enhance memory in mammals, including humans, is disclosed. Such substances include peptides having the amino acid sequence Val-Phe-Phe. Compds. with potential uses as memory enhancers were tested by their effects on learning an avoidance response. The structure and activity relationships were used to determine the topog. for the binding sites for these compds. A potential memory-enhancing substance is designed on the basis of these data.		
ST	amnestic peptide receptor topog model; memory enhancing drug receptor model		
IT	Peptides, biological studies		
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)		
	(amnestic; use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)		
IT	Quantitative structure-activity relationship		
	(memory-affecting; use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)		
IT	Memory, biological		
	Simulation and Modeling, biological		
	(use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)		
IT	Molecular structure-biological activity relationship		
	(memory-affecting, use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)		
IT	67412-83-3	99473-67-3	99896-85-2 107015-83-8 112163-49-2
	134649-29-9	153247-41-7	153247-46-2 153247-53-1
	153287-77-5	163350-37-6	163350-38-7 163350-39-8 163350-40-1
	163350-41-2	163350-42-3	163350-43-4 163350-44-5 163350-45-6
	163350-46-7	163350-47-8	163350-48-9 163350-49-0
	RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)		
	(memory enhancing activity of; use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)		

IT 153247-47-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (peptides containing, as memory enhancers; use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)

IT 134649-29-9

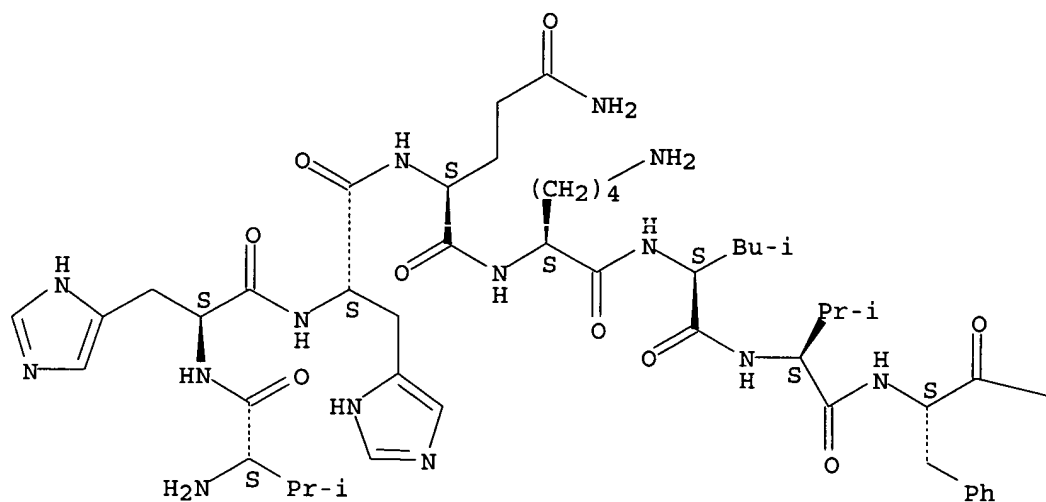
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
 (memory enhancing activity of; use of topog. receptor model to identify binding site for amnestic peptides and design of memory-enhancing drugs)

RN 134649-29-9 HCAPLUS

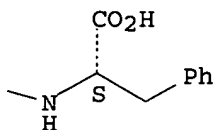
CN L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



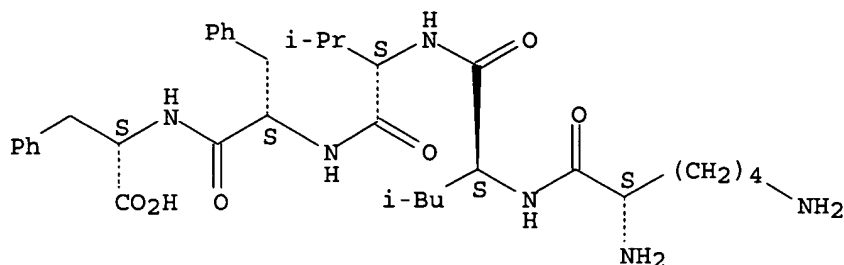
PAGE 1-B



AN 1994:131262 HCAPLUS  
 DN 120:131262  
 ED Entered STN: 19 Mar 1994  
 TI Topography of a binding site for small amnesic peptides deduced from structure-activity studies: relation to amnesic effect of amyloid  $\beta$  protein  
 AU Flood, James F.; Roberts, Eugene; Sherman, Mark A.; Kaplan, Bruce E.; Morley, John E.  
 CS Geriatr. Res. Educat. clin. Cent. (GRECC), St. Louis, MO, 63106, USA  
 SO Proceedings of the National Academy of Sciences of the United States of America (1994), 91(1), 380-4  
 CODEN: PNASA6; ISSN: 0027-8424  
 DT Journal  
 LA English  
 CC 14-10 (Mammalian Pathological Biochemistry)  
 Section cross-reference(s): 1  
 AB Four peptides homologous to amyloid  $\beta$  protein containing the Val-Phe-Phe (VFF) sequence administered intracerebroventricularly after training caused amnesia for footshock active avoidance training in mice. Results with VFF and other peptides containing VFF or portions thereof were used to generate a topog. map for a hypothetical binding surface for amnesic peptides, termed Z. Effects on retention of footshock active avoidance training were rationalized in terms of fit to Z, making possible design of potential memory-modulating peptidic and nonpeptidic substances. Three peptides that neither improved nor impaired retention blocked the amnesic effects of  $\beta$ -(12-28), a peptide homologous to amyloid  $\beta$  protein, opening the way to development of substances that can antagonize the neurotoxic effects of amyloid  $\beta$  protein on neural structures and thus attenuate symptoms and progression of Alzheimer disease.  
 ST amyloid beta protein amnesic peptide  
 IT Amnesia  
 Memory, biological  
 (small peptides related to amyloid  $\beta$  protein mediation of, structure-activity in)  
 IT Proteins, specific or class  
 RL: BIOL (Biological study)  
 (amyloid A4, small amnesic peptides in relation to, structure-activity in)  
 IT Molecular structure-biological activity relationship  
 (memory-affecting, small peptides related to amyloid  $\beta$  protein in)  
 IT 2131-06-8 2577-40-4 3918-90-9 3918-92-1 3918-94-3 53932-31-3  
 64533-12-6 64533-15-9 65111-46-8 67412-83-3 99473-67-3  
 140941-10-2 153247-39-3 **153247-40-6** 153247-41-7  
 153247-42-8 153247-43-9 153247-44-0 153247-45-1 153247-46-2  
 153247-47-3 153247-48-4 153247-49-5 153247-50-8 153247-51-9  
 153247-52-0 153247-53-1 153287-77-5  
 RL: PRP (Properties)  
 (amnesic effect of, structure-activity in, amyloid  $\beta$  protein in relation to)  
 IT **153247-40-6**  
 RL: PRP (Properties)  
 (amnesic effect of, structure-activity in, amyloid  $\beta$  protein in relation to)  
 RN 153247-40-6 HCAPLUS  
 CN L-Phenylalanine, L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L45 ANSWER 29 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN  
 AN 1993:671728 HCAPLUS  
 DN 119:271728  
 ED Entered STN: 25 Dec 1993  
 TI Preparation of pseudopentapeptides with immunomodulating activity  
 IN Degraw, Joseph I.; Almquist, Ronald; Hiebert, Charles; Smith, R. Lane;  
 Uchida, Itsuo  
 PA Japan Tobacco, Inc., Japan  
 SO PCT Int. Appl., 201 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07K005-02  
 ICS C07K007-02; A61K037-02; C07K015-00  
 CC 34-3 (Amino Acids, Peptides, and Proteins)  
 Section cross-reference(s): 1, 15

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9304080	A1	19930304	WO 1992-JP1046	19920819 <--
	W: CA, JP, KR				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
	CA 2094822	AA	19930227	CA 1992-2094822	19920819 <--
	EP 556405	A1	19930825	EP 1992-917987	19920819 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
	JP 06501961	T2	19940303	JP 1993-504226	19920819 <--
PRAI	US 1991-749886	A	19910826	<--	
	US 1992-920601	A	19920803	<--	
	WO 1992-JP1046	W	19920819	<--	

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9304080	ICM	C07K005-02
	ICS	C07K007-02; A61K037-02; C07K015-00

OS MARPAT 119:271728

AB Thymopentin (thypentin) analogs, e.g. R-AA1-AA2-AA3-AA4-AA5-R1 [AA1 = L- or D-Arg; AA2 = optionally N-C1-6 alkylated L- or D-basic amino acid residue, a neutral/nonarom. amino acid residue, or Pro; AA3 = L- or D-Asp or Glu optionally esterified with C1-6 alkyl; AA4 = L- or D-neutral/nonarom. amino acid residue; AA5 = optionally N-C1-6 alkylated L- or D-neutral/nonarom. amino acid residue (wherein one or more H's of its aromatic portion can be substituted by NO2 or halo) or L- or D-neutral/nonpolar/large/nonarom. amino acid residue; R = C1-6 acyl, arylsulfonyl, alkylsulfonyl, arylalkylsulfonyl, alkoxycarbonyl; R1 = OH, NR2R3 (wherein R2, R3 = H, C1-6 alkyl), OR4 (R4 = C1-6 alkyl); wherein at least one of the linkages AA1-AA2, AA2-AA3, AA3-AA4, and AA4-AA5 is a modified peptide linkage selected from COCH2, CH(OH)CH2, and CH2NH and the remaining linkages are CONH or CONMe], useful for the treatment of autoimmune and infectious diseases (e.g. arthritis), are prepared Thus,

coupling of a Grignard reagent  $\text{PhCH}_2\text{CH}(\text{CH}:\text{CH}_2)\text{CH}_2\text{MgBr}$  (preparation given) with N-trityl-L-valine 2-mercaptopyridine ester (preparation given) in THF at 50-60° for 2 h followed by N-deprotection with p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H in MeCN and N-protection with (Me<sub>3</sub>CO)<sub>2</sub>CO in CH<sub>2</sub>Cl<sub>2</sub> containing Et<sub>3</sub>N gave N-tert-butoxycarbonyl-6-amino-7-methyl-3-benzyl-1-octen-5-one. Oxidation of the latter with RuO<sub>2</sub>.xH<sub>2</sub>O/NaIO<sub>4</sub> in aqueous acetone gave 5-N-tert-butoxycarbonylamino-6-methyl-2-benzyl-4-oxoheptanoic acid which was bound to a Merrifield chloromethyl resin and underwent solid-phase peptide coupling with Boc-Lys(ClZ)-Asp(OcHex)-OH (ClZ = 2-chlorobenzylloxycarbonyl, cHex = cyclohexyl) (preparation given) and Boc-Arg(Tos)-OH using DCC and hydroxybenzotriazole to give, after deprotection and resin cleavage, H-Arg-Lys-Asp-Val(k)Phe-OH [wherein (k) indicates the linkage COCH<sub>2</sub> as a replacement for CONH] (I). In a competitive binding assay, I at 10<sup>-3</sup> and 10<sup>-4</sup> M in vitro reduced the mean total count of tritiated thymopentin bound to CEM cells from 3,078 cpm (in the absence of a competitor) to 844 cpm vs. 1,150 cpm for non-radiolabeled thymopentin. The peptide analogs in vitro also increased the release of cyclic GMP in CEM cells, the production of Thy-1 antigens in spleen cells of nu/nu mice, and the serum half-life in mouse and human serum.

- ST pseudopentapeptide prepn immunomodulating activity; autoimmune treatment pseudopentapeptide; infectious disease treatment pseudopentapeptide; thymopentin thypentin analog prepn immunomodulator
- IT Immunostimulants  
Immunosuppressants  
(pseudopentapeptide thymopentin analogs)
- IT Autoimmune disease  
Infection  
(treatment of, pseudopentapeptide thymopentin analogs for)
- IT Inflammation inhibitors  
(antiarthritics, pseudopentapeptide thymopentin analogs)
- IT Peptides, preparation  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(penta-, pseudo-, thymopentin analogs, preparation of, as immunomodulator)
- IT 72210-37-8P 151012-26-9P 151012-27-0P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, in preparation of immunomodulating pseudopentapeptide thymopentin analog)
- IT 151011-32-4P 151011-34-6P 151011-36-8P 151011-37-9P 151011-39-1P  
151011-41-5P 151011-43-7P 151011-45-9P 151011-47-1P 151011-49-3P  
151011-51-7P 151011-53-9P 151011-54-0P 151011-55-1P 151011-57-3P  
151011-59-5P 151011-61-9P 151011-62-0P 151011-64-2P 151011-65-3P  
151011-67-5P 151011-69-7P 151011-70-0P 151011-71-1P  
151011-72-2P 151011-73-3P 151011-74-4P 151011-75-5P 151011-76-6P  
151011-77-7P 151036-34-9P 151036-36-1P 151036-37-2P 151121-46-9P  
151121-48-1P 151121-50-5P 151121-52-7P 151121-54-9P 151121-56-1P  
151121-58-3P 151121-60-7P 151121-62-9P 151121-64-1P 151121-66-3P  
151121-67-4P 151121-69-6P 151121-71-0P 151121-72-1P 151121-75-4P  
151121-77-6P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as immunomodulator)
- IT 962-39-0P, L-Phenylalanine benzyl ester 63628-63-7P 78314-61-1P  
80514-64-3P 80622-02-2P 82068-75-5P 89760-63-4P 103143-66-4DP,  
MBHA resin-bound 139033-47-9P 151011-78-8P 151011-79-9P  
151011-80-2P 151011-81-3P 151011-82-4P 151011-83-5P 151011-84-6P  
151011-85-7DP, Resin-bound 151011-86-8DP, Resin-bound 151011-87-9P  
151011-88-0P 151011-89-1DP, Resin-bound 151011-89-1P 151011-90-4P  
151011-91-5P 151011-92-6P 151011-93-7P 151011-94-8P 151011-95-9P  
151011-96-0P 151011-97-1DP, Resin-bound 151011-99-3DP, Resin-bound  
151012-00-9P 151012-01-0P 151012-02-1P 151012-03-2P 151012-04-3P  
151012-05-4P 151012-06-5P 151012-07-6P 151012-08-7P 151012-09-8P  
151012-10-1P 151012-11-2DP, Resin-bound 151012-11-2P 151012-12-3P  
151012-13-4P 151012-14-5P 151012-15-6P 151012-16-7P 151012-17-8P

151012-18-9P 151012-19-0P 151012-20-3P 151012-21-4P 151012-25-8P  
 151036-38-3P 151036-39-4P 151036-40-7P 151036-41-8P 151036-42-9P  
 151121-73-2P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as intermediate for immunomodulating pseudopentapeptide thymopentin analog)

IT 50-00-0, Formaldehyde, reactions 56-41-7, L-Alanine, reactions 72-18-4, L-Valine, reactions 76-83-5, Trityl chloride 115-11-7, Isobutylene, reactions 334-88-3, Diazomethane 541-16-2, Di-tert-butyl malonate 542-69-8, 1-Iodobutane 542-92-7, Cyclopentadiene, reactions 1155-64-2 1738-78-9 2177-63-1 2637-34-5, 2-Mercaptopyridine 2812-46-6, L-Proline tert-butyl ester 3392-10-7 6638-79-5, N,O-Dimethylhydroxylamine hydrochloride 6921-34-2, Benzylmagnesium chloride 13734-34-4D, resin-bound 13734-34-4D, p-methylbenzhydrylamine resin-bound 13734-41-3 13836-37-8 14611-34-8 15761-38-3 21657-35-2D, resin-bound 24424-99-5, Di-tert-butyl dicarbonate 30794-77-5, 1,4-Dibromobutene 31950-55-7, 1-Bromo-2-methyl-3-butene 50774-73-7, 4-Methyl-3-bromomethyl-1-pentene 54613-99-9 57096-11-4 73821-95-1, N-tert-Butoxycarbonyl-L-aspartic acid  $\beta$ -cyclohexyl ester 73995-27-4 107304-39-2 151012-22-5, L-Aspartic acid benzhydryl ester 151012-23-6

RL: RCT (Reactant); RACT (Reactant or reagent)

(reaction of, in preparation of immunomodulating pseudopentapeptide thymopentin analog)

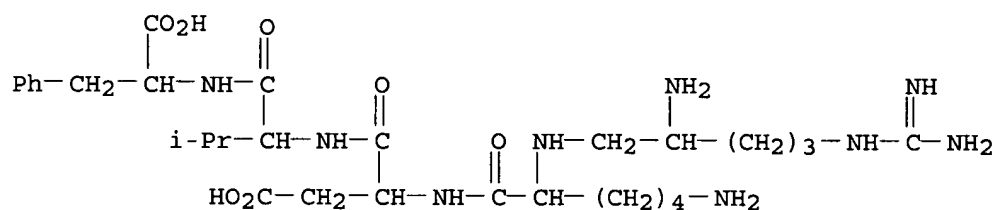
IT 151011-70-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, as immunomodulator)

RN 151011-70-0 HCAPLUS

CN L-Phenylalanine, N-[N-[N-[N2-[2-amino-5-[(aminoiminomethyl)amino]pentyl]-L-lysyl]-L- $\alpha$ -aspartyl]-L-valyl]-, (S)- (9CI) (CA INDEX NAME)



L45 ANSWER 30 OF 30 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1991:427112 HCAPLUS

DN 115:27112

ED Entered STN: 27 Jul 1991

TI Amnestic effects in mice of four synthetic peptides homologous to amyloid  $\beta$  protein from patients with Alzheimer disease

AU Flood, James F.; Morley, John E.; Roberts, Eugene

CS VA Med. Cent., St. Louis, MO, 63106, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1991), 88(8), 3363-6

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

CC 14-10 (Mammalian Pathological Biochemistry)

AB Immediate post-training intracerebroventricular administration of a synthetic peptide homologous to  $\beta$ -protein of brain amyloid, [Gln11] $\beta$ -(1-28), caused amnesia for footshock active avoidance training in mice in a dose-dependent fashion. This effect was specific to memory processing since the peptide did not cause amnesia when injected 24 h after training nor did it disturb storage or retrieval of older memories. Shorter fragments of the amyloid  $\beta$ -protein consisting of

residues 12-28, 18-28, and 12-20 also were amnestic when given intracerebroventricularly, residues 12-20 being least effective. The hippocampus, a brain structure importantly involved in learning and memory, consistently shows severe pathol. changes and deposition of amyloid in patients with Alzheimer disease. Immediate post-training bilateral intrahippocampal injection of [Gln11] $\beta$ -(1-28) produced amnesia at much lower doses than did [Gln11] $\beta$ -(1-28) injected intracerebroventricularly. Thus these exptl. results suggest a possible direct role of amyloid  $\beta$ -protein or fragments thereof in an aspect of the spectrum of cognitive deficit in Alzheimer disease.

ST Alzheimer amyloid beta peptide amnesia

IT Amnesia

(from peptides homologous to amyloid  $\beta$ -protein of humans with Alzheimer disease)

IT Mental disorder

(Alzheimer's disease, amyloid  $\beta$ -protein from humans with, synthetic peptides homologous to, amnestic effect of)

IT 106686-61-7 107015-83-8 112163-49-2 **134649-29-9**

RL: PRP (Properties)

(amnestic effect of, as homolog of amyloid  $\beta$ -protein from humans with Alzheimer disease)

IT **134649-29-9**

RL: PRP (Properties)

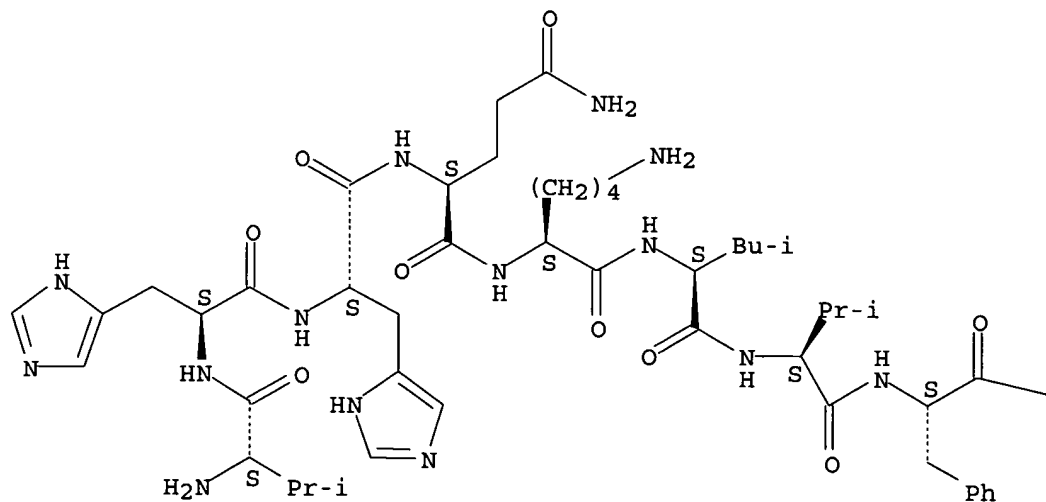
(amnestic effect of, as homolog of amyloid  $\beta$ -protein from humans with Alzheimer disease)

RN 134649-29-9 HCAPLUS

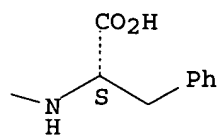
CN L-Phenylalanine, L-valyl-L-histidyl-L-histidyl-L-glutaminyl-L-lysyl-L-leucyl-L-valyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



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